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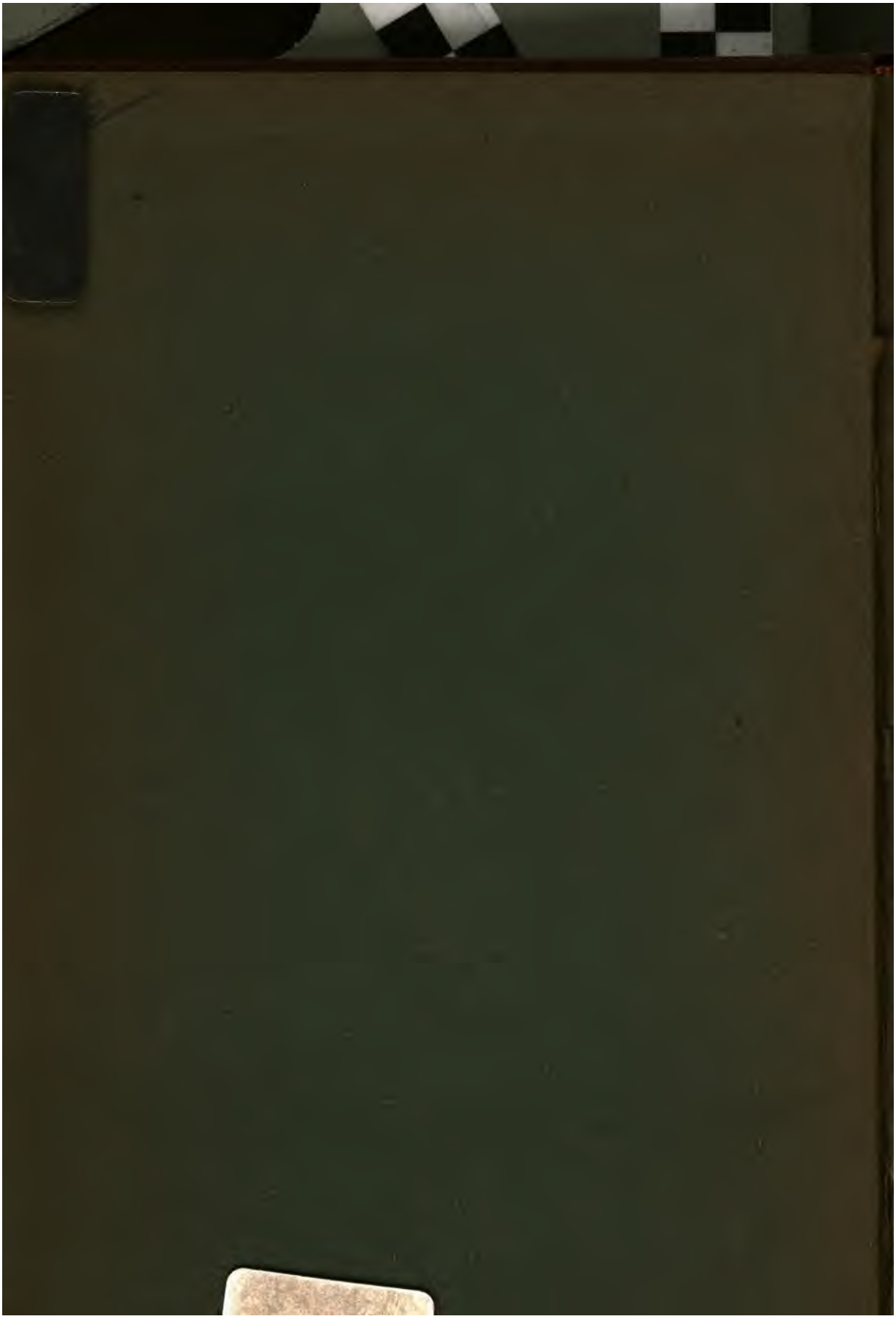

# TRANSACTIONS

OF THE

# American Therapeutic Society

1910

EDITOR

P. BRYNBERG PORTER, A.M., M.D.

PHILADELPHIA
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# ROSTER, JUNE, 1910.

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|---|---|---|
| Anders, James M. | 1605 Walnut St. | Philadelphia, Pa. |
| Anderson, Harry Bertram | 184 Bloor St., E. | Toronto, Canada |
| Ashton, Thomas G. | 1814 S. Rittenhouse Sq. | Philadelphia, Pa. |
| Babcock, W. Wayne | 2033 Walnut St. | Philadelphia, Pa. |
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| Beck, Carl | 37 E. 61st St. | New York, N. Y. |
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| Bracken, Henry Martyn | 1010 4th St., S. E. | Minneapolis, Minn. |
| Britton, Lewis | 1933 Spruce St. | Philadelphia, Pa. |
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| Brown, Philip King | 350 Post St. | San Francisco, Cal. |
| Campbell, William A. | 424 N. Nevada Ave. | Colorado Springs, Colo. |
| Chappell, J. W. | 3907 Grant Road | Washington, D. C. |
| Cheney, Benj. Austin | 404 Whitney Ave. | New Haven, Conn. |
| Coe, Henry Clarke | 8 W. 76th St. | New York, N. Y. |
| Cohen, Solomon Solis- | 1525 Walnut St. | Philadelphia, Pa. |
| Craigin, George A. | 18 Hereford St. | Boston, Mass. |
| Crofton, Alfred C. | 100 State St. | Chicago, Ill. |
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| Fotheringham, John Taylor | 20 Wellesley St. | Toronto, Canada |
| Fox, L. Webster | 1304 Walnut St. | Philadelphia, Pa. |
| Fussell, M. Howard | 421 Lyceum Ave. | Philadelphia, Pa. |
| Gallant, A. Ernest | 540 Madison Ave. | New York, N. Y. |
| Gerrish, Frederic Henry | 675 Congress St. | Portland, Me. |
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| Gordinier, Hermon C. | 89 4th St. | Troy, N. Y. |
| Gordon, Andrew R. | 345 Bloor St., W. | Toronto, Canada |
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| Green, Charles Lyman | 150 Lowry Arcade | St. Paul, Minn. |
| Hall, Arthur J. | 928 I St., N. W. | Washington, D. C. |
| Hall, J. N. | 308 Jackson Block | Denver, Colo. |
| Hibbs, Russell A. | 130 E. 36th St. | New York, N. Y. |
| Hughes, Chas. Hamilton | 3872 Washington Boulevard | St. Louis, Mo. |
| Johnson, H. L. E. | 1821 Jefferson Place | Washington, D. C. |
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| King, Alfred | 610 Congress St. | Portland, Me. |
| Kolipinski, L. | 631 I St., N. W. | Washington, D. C. |
| Leech, D. Olin | 1237 Mass. Ave., N. W. | Washington, D. C. |
| Long, Eli H. | 1335 Main St. | Buffalo, N. Y. |

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| Marple, Wilbur B. | 46 W. 53d St. | New York City. |
| McPhedran, Alexander | 151 Bloor St. | Toronto, Canada |
| Meyers, Campbell | 72 Heath St. | Toronto, Canada |
| Morgan, Francis P. | 3445 Mt. Pleasant St., N. W. | Washington, D. C. |
| Morris, Robert T. | 616 Madison Ave. | New York, N. Y. |
| Morton, William James | 19 E. 28th St. | New York, N. Y. |
| Nammack, Charles Edward | 42 E. 29th St. | New York, N. Y. |
| O'Donovan, Charles | 102 Read St. | Baltimore, Md. |
| Osborne, Oliver Thomas | 252 York St. | New Haven, Conn. |
| Packard, Francis R. | 304 S. 19th St. | Philadelphia, Pa. |
| Patterson, Ross V. | 314 S. 16th St. | Philadelphia, Pa. |
| Pedersen, James | 20 E. 46th St. | New York, N. Y. |
| Pfaff, Franz | 871 Boylston St. | Boston, Mass. |
| Pfahler, George E. | 1321 Spruce St. | Philadelphia, Pa. |
| Pool, Benj. G. | 945 R. I. Ave., N. W. | Washington, D. C. |
| Porter, P. Brynberg | 128 W. 84th St. | New York, N. Y. |
| Porter, William H. | 1674 Broadway | New York, N. Y. |
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| Randolph, Robert Dawson | 396 Bloor St., W. | Toronto, Canada |
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| Rottenberg, Ignatz M. | 105 W. 118th St. | New York, N. Y. |
| Roussel, Albert E. | 2108 Pine St. | Philadelphia, Pa. |
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| Shoemaker, J. V. | 1805 Walnut St. | Philadelphia, Pa. |
| Shoup, Jesse | 2d and Md. Ave., N. E. | Washington, D. C. |
| Small, H. Beaumont | 150 Laurier Ave. | Ottawa, Canada |
| Smith, Oliver C. | 44 High St. | Hartford, Conn. |
| Spenzer, John George | 1825 E. 31st St. | Cleveland, Ohio |
| Sprigg, Wm. M. | 1015 16th St., N. W. | Washington, D. C. |
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| Stoll, Henry Farnum | 417 Albany Ave. | Hartford, Conn. |
| Taylor, John Madison | 1504 Pine St. | Philadelphia, Pa. |
| Thornton, Edward Linn | 922 Spruce St. | Philadelphia, Pa. |
| Van der Veer, Albert | 38 Eagle St. | Albany, N. Y. |
| Van Rensselaer, Howard | 123 State St. | Albany, N. Y. |
| Wheatley, Frank George | 174 North Adams St. | North Abington, Mass. |
| White, John Blake | 1013 Madison Ave. | New York, N. Y. |
| Wilcox, Reynold Webb | 679 Madison Ave. | New York, N. Y. |
| Wiley, Harvey W. | Cosmos Club | Washington, D. C. |
| Wilson, Frederick Morse | 834 Myrtle Ave. | Bridgeport, Conn. |
| Wilson, James C. | 1509 Walnut St. | Philadelphia, Pa. |
| Wood, H. C., Jr. | 434 S. 44th St. | Philadelphia, Pa. |

## HONORARY MEMBERS.

| | |
|---|---|
| Brunton, Sir Lauder | London, England |
| Marshall, C. R. | Dundee, Scotland. |
| Tillmanns, Hermann | Leipsic, Germany |
| Schoeler, Heinrich | Berlin, Germany |
| Hayem, Georges | Paris, France |

## DECEASED MEMBERS

Samuel Claggett Busey, M.D., LL.D., died Oct. 19, 1899.
William P. Manning, M.D., died Feb. 9, 1901.
John Thomas Winter, M.D., LL.D., died June 22, 1902.
George Edward Tyler, M.D., died July 7, 1902.
Robert Henderson Graham, M.D., died Aug. 24, 1903.
George Bingham Fowler, M.D., died March 6, 1907.
John S. McLain, M.D., died June 2, 1907.
Robert Reyburn, M.D., died March 25, 1909.
Justin Steer, M.D., died April 20, 1910.
Howard H. Barker, M.D., died May 8, 1910.

# CONSTITUTION AND BY-LAWS.

## ARTICLE I.

This Society shall be known as the American Therapeutic Society.

## ARTICLE II.

The object of this Society shall be the promotion of therapeutics in its broadest sense.

## ARTICLE III.

This Society shall meet annually at such time and place as the Council may determine.

## ARTICLE IV.

SECTION 1. This Officers of this Society shall consist of a President, three Vice-Presidents, a Secretary, a Treasurer, and a Council of fifteen members, all to be elected from the active membership, by ballot, at an annual meeting.

SECTION 2. The Council may be convened at any time by the Chairman, at the request of any three of its members. Its decisions shall be equivalent to acts of the Society, and shall be reported to it at the next regular meeting. The Council shall elect from its members a Committee on Admissions to consist of three members.

SECTION 3. A vacancy occurring in any office may be filled by the Council.

## ARTICLE V.

SECTION 1. This Society shall consist of not more than one hundred active members. Honorary members may be elected on recommendation of the Council.

SECTION 2. Any qualified physician engaged in the general or special practice of medicine or surgery, or in laboratory research of interest in the treatment of disease, is eligible for membership.

SECTION 3. Applications for membership should be made in writing at least one month before the annual meeting. They are to be referred to the Committee on Admissions, which shall, on approval, present their names to the Society at the annual meeting. Five negative ballots shall reject an applicant.

SECTION 4. Applications for membership shall be accompanied by the annual dues for the ensuing year.

SECTION 5. Resignation of members shall not be accepted until all dues have been paid.

## ARTICLE VI.

All proposed changes of the Constitution must be offered in writing at a regular meeting. They are to be considered only at an annual meeting, when a two-thirds vote of the members present shall be necessary for their adoption.

# BY-LAWS.

1.

The *President* shall preside at the annual meeting of the Society, and deliver an address. He shall appoint a Committee on Scientific Business and a Committee of Arrangements.

In the absence of the President, one of the Vice-Presidents shall preside.

2.

The *Secretary* shall keep a record of the transactions of the Society and of its Committees, conduct all correspondence of the Society, and mail to each member a programme of the meeting, at least two weeks before it is held. The records, publications and seal of the Society shall be in his custody.

The *Treasurer* shall collect all moneys due the Society, disburse the same, as directed by the Council, keep a proper account of all his transactions, and render an annual statement to the Society. He shall have charge of all property belonging to the Society not otherwise provided for.

3.

Ten active members shall constitute a quorum for the transaction of business.

4.

SECTION 1. The *Council* shall constitute a standing committee to consider all matters of interest to the Society. It shall elect a Chairman, Vice-Chairman and a Secretary, and shall appoint an Editor of the Transactions.

SECTION 2. Three members of the *Council* shall be elected annually by the Society, each to serve five years.

SECTION 3. Five members shall constitute a quorum.

5.

The *Committee on Admissions* shall investigate the qualifications of applicants and report at the next annual meeting.

6.

Charges against any member must be made in writing. They shall be referred to the *Council* for investigation.

7.

No papers, report, abstract or other communication, either written or verbal, which, directly or indirectly, commends or advocates any secret, patented or trade-marked product or method of treatment shall be presented to or received by the Society; nor shall any discussion on such product or method be permitted.

Papers are limited to twenty minutes and discussions to five minutes.

8.

The *annual dues* shall be five dollars, payable in advance.

9.

The *order of business meetings* shall be as follows:

1. Reading of Minutes.
2. Reports of Officers and Committees.
3. Election of Members.
4. Presentation of Communications.
5. Miscellaneous Business.
6. Election of Officers.

## REPORT OF THE COMMITTEE ON COMPETITIVE THERAPEUTIC RESEARCH.

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On recommendation of the Council of the American Therapeutic Society, at the meeting of the Society held in Washington, D. C., May 7, 1910, it was voted that an annual prize of one hundred dollars ($100.00) be awarded to the best report on a subject of Therapeutic Research, and the undersigned were appointed a Committee to define the conditions of the competition. We report as follows:

1.—The competition is to be limited to members of the Society in good standing.

2.—The subject of the competition is to be limited to a substance or preparation which is official in the United States Pharmacopœia.

3.—The research may be either wholly laboratory or clinical, or laboratory and clinical combined.

4.—The reports must be (*a*) designated by a distinctive word or motto, and (*b*) must be accompanied by a sealed envelope marked with the said word or motto, and containing the name and address of the competitor and of the laboratories or hospitals in which the research was conducted. (*c*) The report and protocol must be typewritten. (*d*) These must be in the hands of the Chairman of the Council before April 1, 1911.

5.—The reports and protocols are to be judged by a Committee consisting of the Vice-Presidents of the Society, who shall decide which is the best report as showing valuable therapeutic research, and shall return their decision, together with all the papers submitted to them, to the Chairman of the Council before May 1.

6.—The Chairman of the Council shall then return the unsuccessful reports to their authors, and shall notify the successful author.

7.—The successful report shall be read by the author on the first day of the meeting, immediately after the President's address.

8.—All matters connected with the competition shall be considered as absolutely confidential by the Chairman of the Council and the Vice-Presidents, except as to the successful competitor.

9.—The Vice-Presidents as judges may divide the prize, or not award it in case no competition is deemed of sufficient merit.

10.—In case any Vice-President shall fail to act, the President of the Society shall be added to the Committee.

Signed: Reynold Webb Wilcox,
Thomas E. Satterthwaite,
Spencer L. Dawes,
Committee.

# LIST OF PAPERS READ BEFORE THE SOCIETY.*

ANDERS, J. M.—What Constitutes a Useful Drug, and Shall the Preparations of a Useful Drug be Limited to One or Two? Read by title. (*Monthly Cyclopædia and Medical Bulletin*, Feb., 1911.)

BABCOCK, W. W.—The Range of Activity and the Untoward Effects of Certain Spinal Analgesics; Based on Two Thousand Administrations (1910).

BARNES, N. P.—Bacterins: their Present Status in Therapeutics (1910).

BARTON, W. M.—Hexamethylenamine in the Treatment of Otitis Media (1910).

BECK, C.—On Morbus Basedowi. Read by title (1910).

BEEBE, S. P.—The Preparation of Thyroid Gland for Use (1910).

COHEN, S. S.—What Unofficial Drugs are of Sufficient Clinical Value to be Recognized in the United States Pharmacopœia of 1910? Read by title.

DA COSTA, J. C., JR.—The Routine Use of the Autogenous Vaccines (Bacterins) in the German Hospital, Philadelphia (1910).

DAVIS, N. S., JR.—Should the Pharmacopœia Contain Only Useful and Efficient Drugs? (*Monthly Cyclopædia and Medical Bulletin*, Feb., 1911).

FISHER, E. D.—Senile Epilepsy. (*Monthly Cyclopædia and Medical Bulletin*, September, 1910.)

FLICK, L. F.—Skin Inunctions as a Therapeutic Measure. Read by title. (*Monthly Cyclopædia and Medical Bulletin*, August, 1910.)

FUSSELL, M. H.—Further Consideration of the United States Pharmacopœia. Read by title. (*Monthly Cyclopædia and Medical Bulletin*, Mar., 1911.)

GALLANT, A. E.—The Delayed Menopause: its Dangers and Therapeutic Indications. (*New York Medical Journal*, June 18, 1910.)

GREEN, C. L.—Asthenia Universalis Congenita. (*American Journal of the Medical Sciences*, 1910.)

KEBLER, L. F.—The Present Status of Drug Addictions in the United States. (*Monthly Cyclopædia and Medical Bulletin*, Jan., 1911.)

KING, A.—Further Study of Diabetes as an Infectious Disease. (*Monthly Cyclopædia and Medical Bulletin*, July, 1910.)

KOLIPINSKI, L.—Further Use of Solution of Calcium Creosote in Medicine. (*Monthly Cyclopædia and Medical Bulletin*, August, 1910.)

LONG, E. H.—The Metric System. Read by title. (*Monthly Cyclopædia and Medical Bulletin*, Mar., 1911.)

MCPHEDRAN, A.—Treatment of Pneumonia. (*Monthly Cyclopædia and Medical Bulletin*, June, 1910.)

MORGAN, F. P.—Suggestions for the Pharmacopœia of 1910: A Brief Consideration of the Subject in its Relation to the Federal Food and Drugs Act. (*Monthly Cyclopædia and Medical Bulletin*, Mar., 1911.)

MORRIS, R. T.—Surgery of the Obese. Read by title. (*Monthly Cyclopædia and Medical Bulletin*, 1910.)

OSBORNE, O. T.—U. S. P., 1910. How May It Be Constructed? (*Monthly Cyclopædia and Medical Bulletin*, Jan., 1911.)

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* For list of papers read before the Society from its organization to the year 1909, inclusive, see the *Transactions* for 1909.

REMINGTON, J. P.—Revision of the United States Pharmacopœia. (*Monthly Cyclopædia and Medical Bulletin*, Feb., 1911.)

ROSS, GEORGE G.—A Case of Recurrent Abscess Formation, Due to Staphylococcus Infection, Successfully Treated by Autogenous Vaccines. Read by title. (*Monthly Cyclopædia and Medical Bulletin*, September, 1910.)

SATTERTHWAITE, T. E.—High Frequency Currents in the Treatment of Arteriosclerosis. (*Medical Record*, July 2, 1910.)

SHOOK, F. N.—The Malarial Infections and Their Treatment in the Canal Zone. (*Monthly Cyclopædia and Medical Bulletin*, June, 1910.)

SHOUP, J.—Immediate and After Management of the Puerperant. (*Monthly Cyclopædia and Medical Bulletin*, October, 1910.)

STEWART, F. E.—Some Points in Bacterial Therapy. (*Monthly Cyclopædia and Medical Bulletin*, October, 1910.)

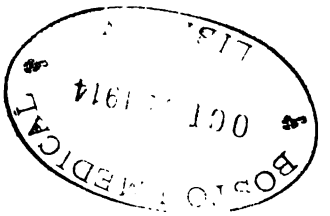
TAYLOR, J. M.—Some Principles in the Treatment of Chronic Nervous Diseases. Read by title (1910).

WHITE, J. B.—Important Therapeutic Indications in the Treatment of Typhoid Fever (1910).

WILCOX, R. W.—The Treatment of Leukæmia by the Röntgen Ray. (*Monthly Cyclopædia and Medical Bulletin*, July, 1910.)

WILLIAMS, T. A.—The Treatment of "Parasyphilis" of the Nervous System in the Light of Recent Research: Paresis and Tabes Dorsalis. (*Monthly Cyclopædia and Medical Bulletin*, Dec., 1910.)

WILSON, J. C.—President's Address. The Progress of Therapeutics. (*Monthly Cyclopædia and Medical Bulletin*, June, 1910.)



# SCIENTIFIC PROCEEDINGS.*

## ELEVENTH ANNUAL MEETING,

## Held at the Hotel Raleigh, Washington, D.C., May 5, 6 and 7, 1910.

The address of welcome was delivered by DR. HARVEY W. WILEY, Washington, D. C., and Dr. Alexander McPhedran, Toronto, Canada, responded for the visiting members.

### PRESIDENT'S ADDRESS: THE PROGRESS OF THERAPEUTICS.

BY J. C. WILSON, M.D.,

Professor of Practice of Medicine and Clinical Medicine in Jefferson Medical College, PHILADELPHIA.

THE advance of the art of healing has been compared to that of a drunken man, who steps with an uncertain gait, now turning this way and that, now reeling or stopping altogether, and after many slow and tortuous steps too often failing wholly to arrive at his destination. The student of the history of medicine finds this simile false in almost every particular. The progress of our art is rather to be compared to the course of a river in a new channel through a broken and hilly land. It has met with many obstacles both great and small, but all difficult to overcome—now an inviting course, which has proved to be no thoroughfare; now an alluring byway which has led to nothing; again, rocky barriers and insurmountable heights which have turned it aside to await, in drowsy hollows and unproductive marshes, the flooding of new waters and the massing of new energies to help it to attain its end and to flow, a powerful and beneficent stream, toward the great accumulated sea of human knowledge. To relate the story of this progress from the myths which surround the head of Æsculapius to the cold facts of the laboratory of our day to an audience such as I have the honor of addressing would be to rehearse a twice-told tale; nor would

* It is to be understood that the Society does not hold itself responsible for any views expressed by the readers of papers or participants in discussions.

A list of all the papers read before the Society up to the present year, arranged under the names of their respective authors, will be found in the *Transactions* for 1909.

time permit, nor the slender learning possible in the strenuous life of the physician of our day. To do it worthily would be the telling of the strangest and most moving romance of history, in which superstition and credulity, craft and avarice, ignorance and vice have waged through the centuries a losing warfare against the finest and most noble attributes of mankind, the observation of nature, scientific truthfulness, unwearying devotion to human welfare, the purest altruism and the highest exercise of reason in the struggle for the maintenance of health, the mitigation of suffering and sorrow, and the prolongation of life.

In this history are many leaders of men whose lives, devoted to the work of their day, have moulded and impressed the thought of the remotest periods even to our time. Foremost stands Hippocrates, well called the father of medicine, in whose writings are reflected the literary grace and philosophical spirit of the most enlightened age of Greece. Hear the first of the aphorisms. We never tire of it. "Life is short, art is long, occasion sudden, to make experiments dangerous, judgment difficult. Neither is it sufficient that the physician do his office, unless the patient and his attendants do their duty and that externals are well ordered." This in the island of Cos, in the Ægean Sea, 400 years B.C., by one who has the great distinction of having been the first to put aside the traditions of ignorance and superstition and to found the practice of medicine upon the phenomena of nature. Next in the course of time conspicuous is Claudius Galenus of Pergamus, whose skill as an anatomist and voluminous writings upon medicine made him the master authority upon medical knowledge for centuries.

From the time of Galen history was long silent upon the subject of medicine. The teachings of the Hippocratic school were kept alive chiefly by the Saracens, who, however, added little to the knowledge previously acquired. To this period belong Oribasios and Avicenna. The so-called Arabic period extended to the time when, under the influence of the Crusades, the Renaissance began. Europe, at first gradually, then with a start, aroused from the lethargy of a thousand years. Schools of learning and universities sprang up in Salernum, Naples, Montpellier, Paris, Oxford, Bologna. Within two centuries almost every important city of Europe had its university. The faculties of theology, arts, law, and medicine were gradually differentiated. But medicine was prominent in every school. In some, as Salernum, medicine was long the sole department, a suggestive commentary upon modern university organization, in which are found sometimes all the faculties represented except that of medicine; or, again, a medical department dragging on an unsatisfactory existence by reason of inadequate equipment and a discouraged and not altogether harmonious faculty.

A period of great activity in medicine followed. Students flocked from one university to another to listen to the teachings of the popular professors. This was the time of the great early anatomists, Lisfranc, Mondino, Linacre, Sylvius, Vesalius, and the famous succession which culminated toward the close of the sixteenth century in Harvey, who by the discovery of the circulation and the demonstration of the correlation between function and structure signalized the dawn of scientific medicine.

Skillful as the anatomists of this period were they failed to recognize the underlying principle of their art, and it remained for the indefatigable Bichat, a genius of the first order, two centuries later to demonstrate the identity of membranes and tissues in the different organs and to develop the science of general anatomy, just as it had been left to the early microscopists to recognize the cell as the morphological unit of the tissues and create histology, and to Virchow, who was born two decades after Bichat died, to found the science of cellular pathology.

Meanwhile the teachings of Harvey were bearing fruit in various directions. Morgagni showed anatomy to be the basis of all other medical studies and became the founder of pathological anatomy. Boerhaave, the great Hollander, and the English Sydenham were developing medicine from the clinical side and expounding the doctrine of what we now know as the natural history of disease. Haller, who was not only anatomist but likewise poet and statesman, was teaching physiology in Göttingen, and William and John Hunter in London were carrying on researches in the true spirit of science in problems relating to anatomy and physiology, and making practical application of their results in midwifery and operative surgery.

Early in the eighteenth century the time was ripe for a new departure in medicine—the study of causes. The accumulated knowledge of structure and the growing knowledge of function had brought to light in pathological anatomy many of the lesions underlying the derangements of physiological processes which, taken together, constitute the manifestations of disease. The new problems were subtle and difficult. In their solution, and there only, was the progress of medicine possible. Demoniacal possession, an offended deity, spells and witchcraft, causes that had been invoked to account for sickness in the individual and pestilence in the multitude, could no longer, in the growing light of science and the clearer perception of the phenomena of nature, be regarded as adequate or even acceptable. Working hypotheses were not wanting, but the ancient superstitions and vain guesses based upon imperfect observation lay like an incubus upon a pathology struggling into existence, prolonging a blundering empiricism, and postponing the very conception of such a thing as rational therapeutics. To the theory of humoral pathology we owe scarcely anything but meaningless terms which cumber and distort nosology, and measures of treatment mostly abhorrent to nature. William Cullen regarded the nervous system as the primary seat of diseases which were due either to spasm or atony, while his pupil and assistant, John Brown, likewise of the University of Edinburgh, placed all diseases in two great categories, the sthenic, resulting from overexcitation, and the asthenic, arising in consequence of underexcitation. Hahnemann promulgated the theory that knowledge of disease is limited to its signs and symptoms, that it is impossible to know anything of pathological conditions hidden from the eye, and that the removal of morbid manifestations means that the disease which caused them has also been removed. Broussais, of Paris, propounded the so-called physiological system of medicine, which rests upon the hypothesis that, since irritation or excitation is the fundamental attribute of all living animal tissues, diseases are produced by an undue increase in that attribute—a variant of the doctrine of Brown.

These researches in the direction of etiology, having their origin in mere speculation, led to no direct practical results, but they indirectly stimulated renewed investigation in pathological anatomy and clinical medicine. The close of the eighteenth and the first half of the nineteenth century was a period of remarkable activity. Diseases were divided into general and local or constitutional and visceral, a classification which in some instances has been carried out more rigidly for purposes of description and teaching than the facts of nature warrant. The fevers were classed as eruptive, malarial, and continued, and under the teachings of Louis and his pupils the last group was subdivided into typhus, typhoid, and simple. Relapsing and yellow fever, influenza and dengue were recognized as distinct nosological entities and were found in their transmission from the sick to the well to retain their specific characters—a fact that tended greatly to advance the idea of infection and to clear the way, as did the great discovery of Jenner a few years before, for a scientific knowledge of causes. The forms of pulmonary disease were discriminated; pleurisy and pneumonia were separated; diseases of the heart were carefully studied, and Richard Bright, in 1827, called attention to the characteristics of the forms of kidney disease long described under his name, and set our knowledge of them upon a sure basis. Percussion, the *inventum novum* of Auenbrugger, discovered in 1761, forgotten, but revived and amplified by Corvisart, constituted the beginning of physical diagnosis, while auscultation and the invention of the stethoscope by Laennec, and the impetus which they gave to the bedside study of diseases of the lungs, heart, and abdominal viscera, marked an epoch of incalculable importance in the history of clinical medicine.

With the development of pathological anatomy on the one hand and of clinical methods on the other came that division of labor to which we owe the specialties—a concentration of energy which may be compared to intensive farming and which has done more to secure accuracy in scientific observation in clinical work and precision in therapeutic measures than any other event in the history of medicine.

Among the specialties, alienism and neurology were of supreme importance in paving the way for a scientific recognition of the causes of disease, and have had a profound influence upon modern therapeutic thought. But it was to the microscope, which from the time of Galileo, who has been called the greatest of early opticians, till the end of the eighteenth century was scarcely more than a scientific toy, that the study of causes owes its crowning successes. The animalculæ of Leeuwenhoek as supposed causes of disease and the theory of spontaneous generation to which they gave rise so stimulated the development of the instrument itself, microscopic technique, and the spirit of investigation that two centuries later, with the relegation of the former to their proper place in nature and the triumph of the dictum of Harvey, *omne vivum ex ovo,* bacteriology, the youngest of the natural sciences, daughter of the genius of Pasteur and Koch, came into being.

Thus at the beginning of the last third of the nineteenth century the study of causes found a sure foundation in the facts of science, and empiricism in therapeutics gave way to rationalism. Half a century has not yet elapsed and

the art of healing shows signs of being revolutionized. The modern theories of infection and immunity are established upon unassailable facts. The part played by bacteria in nature and the arts is of an importance and extent wholly unsuspected until within the last two or three decades. The part which they play in the causation and cure of disease remains among the mysteries of nature, of which as yet our knowledge is only at the threshold. Many of those which are pathogenic are known to us by specific morphological, tinctorial, and cultural characters, but the existence of others which have eluded the known methods of research may be inferred, as in the case of measles for example, by the constancy of certain associated morbid phenomena, just, to take an illustration from enormous magnitudes, as astronomers have inferred the existence of an undiscovered celestial body from disturbances in the orbit of those which are known.

The blood-serum, not long ago regarded as a simple solution of albumin and certain salts, is now known to possess properties in health and disease of the most subtle and occult characters and potentialities in regard to infection, immunity and therapeusis equally mysterious. The history of the advance of medicine would be but a series of disconnected episodes were it not that it teaches us that here, as in other fields of human endeavor, knowledge ripens slowly and that failures are the stepping stones to success. It teaches us another lesson worth the knowing, namely, that the control of effects can be compassed only through a knowledge of their causes. More than two thousand years of empiricism before reason came to her own in medicine! There were charms and incantations and pilgrimages and votive offerings and laying on of hands, yes, and prayers; but no calamity of plague or pestilence was averted and no man who was really sick was made well. Drugs there were of all kinds, and many of them potent, drastic or sleep-compelling as the case might require, but

> "Not poppies nor mandragora
> Nor all the drowsy syrups of the East"

could touch the ills of mankind at their source. Jenner alone in all time before the era of bacteriology—our era—applied the knowledge of causes to preventive medicine and wrought the wonder of a rescued world. To-day we watch the effects of the antitoxin made possible by the work of Klebs and Loeffler, or those which follow the administration of Flexner's serum, and experience the sensation of having witnessed a miracle. But there are no miracles.

There is yet another lesson in this history of our healing art, namely, the indirection by which it has advanced. There is no reason for medicine except to prevent and cure disease. But most of the actual workers who have made this history appear to have been concerned with something else. It is true that the school of Hippocrates, at Cos, was a great medical center, and the recent work of the archæologists shows that there were splendid buildings, temples perhaps, or it may be hospital pavilions for the care of patients. We do not know. But thither came students in great numbers to study medicine, not to practise it. Galen was physician to the school of gladiators in Pergamus and afterward attended Marcus Aurelius at Venice and in Rome, but he

found time not only to write a great many treatises upon medicine, but many more upon philosophical subjects, and is said to have placed greater faith in amulets than in drugs. The Arabian physicians are generally described as philosophers as well as physicians, and wrote voluminously on logic, metaphysics, astronomy, and geometry. It does not appear that they were great practitioners. In the dark ages of European history such healing as was practised was in the hands of the clergy, who united the functions of the physician with those of the priest. With the Renaissance medicine became again a learned profession, but we find its great men more concerned with anatomy than with sick men yet alive. That arch-charlatan, Paracelsus, who was a contemporary of Harvey, took much interest in actually getting people well, and thereby acquired a high reputation. The translation of Cullen's "Materia Medica" led Hahnemann to write the "Organon of the Art of Healing," and to propagate a system of therapeutics based upon "similars," "dynamization," and infinitesimal doses, irrational in itself but leading to a welcome reaction against the nauseous and disgusting polypharmacy of the times, and from this period there has been less of indirection and a progressively increasing tendency toward practical results.

This tendency was the influence the recognition of which ten years ago brought the American Therapeutic Society into being, and it is this tendency which constitutes the motive and stimulus for its well-organized and effective work. Young among the national societies, this was the first and is the only American national society which has for its sole object the utilization of the late results of time in the prevention and cure of disease. The specialism which has been of so great a service in the art of medicine has rendered a similar but even greater service in the organized medical profession. It has given to the American Medical Association its Sections, to the Congress of American Physicians and Surgeons its constituent Societies, it has distributed a great work among many efficient organizations; but it has left to our Society the supreme task of the application of results to the great purpose of every worker—prevention and cure.

And this leads me to remind you that specialism and organization are complemental: that without the one the other cannot exist and that the new medicine is the product of this union. In the medical sciences individualism has passed away. There will always be leaders, but never again a Hippocrates, nor ever a Galen or Harvey. The greatness of the man of our day is merged in the greatness of his coworkers. Authority and precedent, which are the power of the law, have become as idle words in medicine, which concerns itself with facts and facts alone, having become altogether disdainful of opinions as such.

A comprehensive survey of the work done by the members of this society individually and collectively discovers here also a well-defined tendency to specialism. Three main therapeutic trends have been differentiated. First, the Hippocratic medicine in which the forces of nature other than drugs play the most important rôle. Of predominating influence in the days of classical antiquity, the curative powers of diet, exercise, baths, mineral waters, and

climate fell into a long neglect, to be revived in modern medicine with great advantage to the practice of the therapeutic art. One of our members has edited a series of extremely valuable books upon these subjects. Second, the general subject of psychotherapy and re-education in the management of some of the functional neuroses. This form of treatment, though of later origin, is by no means a modern invention, as many assume it to be. Seneca, who lived at the beginning of the Christian era, is referred to now by writers upon the subject and the curious and ceaseless doubts and fears of psychasthenics of a certain type have been familiar to the clergy from the earliest times. Much wise advice concerning the management of such persons may be found in early ecclesiastical and philosophical literature. It is, however, only in recent years that this method of treatment has been developed and systematized under the leadership of men like Freud and Breuer in Germany, and Taylor and others in our own country. The symposium upon psychotherapy at our meeting in New Haven last year, in which my distinguished predecessor took part, constitutes one of the most important recent contributions to the subject. The third and main trend includes the general study of therapeutics as comprising the empiric use of drugs on the one hand and the rational employment of causal remedies upon the other.

The life-work of the first president of this society has been devoted to experimental therapeutics and the study of the physiological action of drugs, in particular the alkaloids, and throughout its existence the communications to this honorable body have embodied the results of accurate and scientific clinical studies in this field of investigation. Our work consists in the application of the means to the end, and the time is now at hand for us to enter upon the latest phase of applied therapeutics from this point of view, namely, rational therapeutics based upon the latest results of the scientific study of the causes of disease—serum therapy, opotherapy, and the use of bacterins. At our last meeting one of our members whose studies in opotherapy have attracted worldwide attention read a most important communication upon that subject, and our programme for this meeting contains a number of papers upon bacterins.

At an early stage in the progress of therapeutics as an art, it became necessary to publish collections of approved medical formulæ, together with the processes necessary for making the compounds therein described. Such a collection is known as a codex or pharmacopœia. These publications soon received the sanction of national authority in the principal countries. They acquired, in the course of time, an authoritative character and were subjected to revision at stated intervals. The first pharmacopœia, that of Nuremberg, appeared about the middle of the sixteenth century; that of the College of Physicians of London in 1618. Of the latter, eleven editions were issued, the last in 1851. Similar publications were issued under the authority of the organized profession in Dublin and Edinburgh. Since 1858 the British Pharmacopœia, an official publication of the Medical Council, has been the recognized authority in Great Britain. The Prussian Pharmacopœia and the French Codex are generally used in European countries. The first publication

of this character in our own country was issued in Philadelphia in 1778, and a number of others subsequently appeared under the auspices of various medical institutions. As the outcome of the transactions of a convention held at Washington in 1820, "The Pharmacopœia of the United States of America" was published. This publication has been regularly revised at a convention of delegates from various authorized bodies, including the medical departments of the United States army and navy. A convention will be held in this city in a few days for the purpose of the ninth decennial revision of this work. In view of this fact it has appeared appropriate that a symposium upon matters concerning the revision of the Pharmacopœia should form part of the work of the American Therapeutic Society at this meeting. Those who are to take part are men especially interested in the matter, most of them delegates to the approaching convention, and all qualified to speak with authority upon the subjects to be discussed, especially from the standpoint of the practitioner of medicine. It is the confident hope of the members of this society that this discussion will exert an important influence upon the transactions of the convention.

In addition to the work of the members, there will be a number of communications from gentlemen who have accepted the invitation to address us upon therapeutic subjects which have especially engaged their attention and to take part in our discussions. I have the honor to thank those gentlemen all and severally, in the name of the Society, and to extend to them our most cordial greeting.

# THE TREATMENT OF PNEUMONIA.

By ALEXANDER McPHEDRAN, M.D.,
Professor of Medicine, University of Toronto,
TORONTO, ONT.

PNEUMONIA is a local specific inflammation due to a local infection which results from the general infection, the lung being infected through the blood-stream. It is also peculiar in that before the infection, either general or local, betrays its existence the organism has gained a firm foothold in the lung, often affecting a large area of it. This fact has an important bearing on the treatment, especially in reference to the arrest of the disease.

For the last thirty years or more death in pneumonia has been generally regarded as due to cardiac failure in the great majority of instances. The cardiac failure is usually caused by depression of the vasomotor center in the medulla by the toxic albuminoid excreted by the pneumococcus. The failure of the circulation is possibly as much vascular as cardiac. The cases of cardiac failure may be divided into two groups viz.: (1) *The asphyxial,* in which there are cyanosis and other signs indicating failure of the right heart. The great majority of cases belong to this group. (2) *The syncopal,* in which there are the signs of anæmia of all parts, probably caused by splanchnic paresis and consequent dilatation of the abdominal vessels. In these cases the heart, in common with other organs, suffers from anæmia rather than from distention, yet the right ventricle is found at the autopsy to be filled with blood. In both groups the chief aim of treatment should be to raise the blood-pressure by vascular stimulation, in order to restore the circulation and so secure improved nutrition and excretion. The blood-pressure, therefore, becomes the best index as to the treatment which should be carried out. We know of no specific remedy for pneumonia. Although our knowledge of the cause of the disease has greatly increased, little if any advance has been made in its treatment. The mortality from it still remains excessively high, probably even increasing where the population is congested. Is the explanation for this the fact that the air in houses is kept at a much higher temperature than in former times and that the mode of living is growing less and less invigorating?

*Prophylaxis.*—Virulent pneumococci are so frequently present in the mouth that it follows that there must, in health, be strong resisting power in the body fluids. Two diseases are very frequently associated with pneumonia—measles in children and influenza in adults. West's table shows a remarkably close relationship between influenza and pneumonia from 1889, the year of the first epidemic of influenza, down to 1905.[1] Therefore, no one convalescent from influenza should run the risk of chill or over-fatigue

[1] The Practitioner, London, Vol. I, 1908; 430.

until recovery is complete. During the stage following the fever in influenza there is usually subnormal temperature and therefore general depression and lessened resisting power. This subnormal temperature furnishes a valuable index as to the care which should be taken to forestall the occurrence of pneumonia or other infection, to any of which the lessened resisting power increases the liability.

*Curative Treatment.*—Although we have no specific remedy for pneumonia, nevertheless it is hopeful that persevering efforts are being made to discover one. Naturally the trend of investigation is aimed at the discovery of a serum or a vaccine which will arrest the disease or at least moderate and

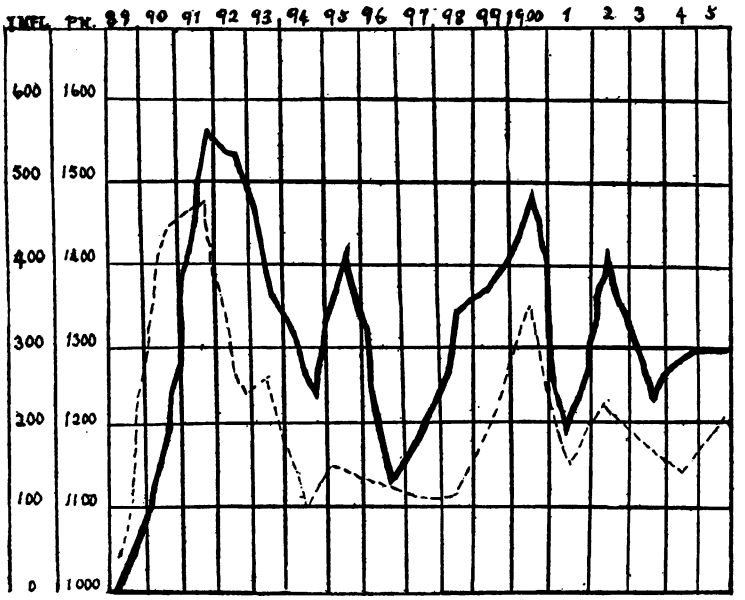



Table showing mortality curve of Pneumonia and Influenza for the years 1889-1905, constructed from the Registrar-General's returns.
.....Influenza. ————Pneumonia.

shorten its course. Thus far not much definite progress has been made. There are various reasons for failure. Antipneumococcic serum is not antitoxic, but antibacterial, and would therefore require to be given at a very early stage of the disease, before the bacteria became firmly lodged, that is, before definite symptoms are excited; but that is before it is possible to make a diagnosis. Then, there are several varieties of pneumococci, and the serum of any variety may be powerless against the invasion of one or more other varieties. The employment of "killed" cocci or vaccines offers an alternative therapy. Eyre, in his interesting article[2] on this aspect of the treatment, says that a considerable measure of success has been attained by this means of treatment. How far it will bear out this estimate of its value remains to be proved by the test of clinical experience. Latham has found pneumococcic vaccine given

2 Allbutt & Rolleston's "System of Medicine," Vol. V, page 241.

by the mouth to have a marked influence on the progress in two cases, and refers to reports of encouraging results from Boellke's vaccine in severe cases of pneumonia and pneumococcic endocarditis. It is not probable, however, that vaccines can have a favorable influence in acute cases, because such patients are already suffering from excessive toxin stimulation. In some the intoxication is so severe as to so depress the hæmopoietic tissues as to paralyze their powers of producing leucocytes, and a fatal termination is the invariable result, while in others, although an excess of leucocytes is discharged into the blood, the patient is so depressed by the toxæmia that his powers soon fail and death is almost as inevitable. To inoculate either of these classes of cases would be to add to their already excessive toxæmia and hasten the fatal ending. In the cases which are able to react successfully against the invasion of the bacteria a vaccine is not only not required, but might so add to the general toxæmia as to exhaust the vitality of the patient. In delayed resolution of the consolidated lung and in circumscribed infections of other parts vaccines may prove of much benefit, as in such cases there is but little general infection; probably not sufficient to excite vigorous reaction in the leucocyte-producing tissues. Vaccines, therefore, appear to have a very limited field in the treatment of pneumonia.

*The symptomatic treatment* or, better, the *treatment of the patient* as indicated by the symptoms.—In ordinary attacks of pneumonia in children and younger adults no active measures are necessary. Rest in bed, sufficient clothing to keep the patient comfortably warm, fresh cool air, light diet in moderation, and cleanliness of mouth and body are sufficient. Early and satisfactory recovery results in all cases unless some untoward circumstance occurs. It is only as there is suffering from distressing or dangerous symptoms that there is need for a resort to special measures for relief and for guarding as far as possible against danger to the vital forces. One of the most efficient means at our disposal to sustain vitality and aid the patient in resisting the depressing influences of the infection is *fresh air,* and, probably better, cold air, because it stimulates respiration and, being more dense, supplies more oxygen in proportion to its volume. In the hospital, except in inclement weather, I have all severe cases placed on the balcony, screened from wind and shaded from too strong a light. The patient is given his food and drink there, but the bed is wheeled into the ward when any other attentions are required. The beneficial effect is often quite marked and soon shown after he is moved out. Usually the breathing is made easier, sleep more restful, the color becomes less cyanotic, the mental state is clearer, and food is taken better and better digested, with less liability of distention of the stomach and bowels. If these effects are produced, the pulse improves, and with the improved circulation there is, no doubt, increased excretion of toxins by the kidneys. The cold air may make the cough more irritating for a time, but this is usually relieved by a mild sedative. No harm can result if the patient is covered, including the head, so as to keep him warm. The disease being of short duration, *diet* is not the important question it is in enteric fever, yet it is desirable that the patient should get food of about

the value of 2000 calories per diem. If there is any appetite, he should be allowed to choose his food so long as his desires are reasonable. If he is seriously ill there is seldom any desire for food; then milk, raw or prepared, or its equivalent, will suffice, but the utmost care should be observed that no abdominal distention results, as often occurs owing to the paretic effect of the toxæmia on the bowel.

The greatest danger in pneumonia is from *toxæmia.* To it are chiefly due the dangers from cardiovascular and respiratory failure, results that are largely attributable to the depressing effect of the toxins on the medullary nerve centers. It is of the first importance to counteract the depression of the nervous system. It is therefore important that the two chief signs of nervous depression, restlessness and insomnia, should be relieved if possible. Many means are resorted to for this purpose, such as the cool or cold pack, spongings, general and cardiac stimulants, and sedatives; of these agencies *opium* is probably the most effective. There is no remedy so generally potent to relieve cardiac failure from any cause, especially in the aged. It should be given as indicated, preferably as morphine hypodermically, and early, while the bronchi are still free, as its use later is liable to lead to accumulation of the bronchial secretion. Marked dilatation of the right auricle, as shown by extension of dullness to the right of the sternum in the fourth interspace, is also a contra-indication. If this is much over a finger breadth the dilatation is serious, and there will be marked dyspnœa, some cyanosis, and increasing bronchial secretion; conditions rendering the use of morphine dangerous, yet in some cases advisable. As to the best means of treating this condition there is much difference of opinion, but all agree that it should be prevented if possible by remedies which stimulate, in the first place, the nerve centers, such as strychnine, atropine and alcohol, and, in the second place, the heart directly, such as digitalis, the caffeine group, and strophanthus; also the application to the præcordium of the ice-bag. The late Dr. Balfour had good results from 10 minims of tincture of digitalis with 10 grains of hydrated chloral, begun early and given three or four times daily. He found that the digitalis prevented depression from the chloral. One of the most potent cardiac stimulants is strophanthin, given intravenously, but this or any other stimulant, in order to be effective, must be given before there is much degeneration of the heart muscle. English physicians generally, and there are no better therapeutists, are much in favor of applying four or five leeches to the right of the sternum as soon as signs of dilatation of the right auricle appear. This leads to the consideration of *venesection* and its indications. Most writers approve of it in robust, full-blooded patients with a strong, high tension pulse. Such patients will bear almost any treatment and will usually "weather the storm" without any aid beyond rest and general care, so that venesection in such cases is seldom a vital question. But what are we to do for those of ordinary vigor, or those even far from being robust, when they show the danger signals of a dilated and dilating right heart? If they are to be saved it must be by prompt, vigorous action; hesitation means failure. The first and urgent indication is to relieve the

tension in the right heart, so that its systole may be effective in expelling its blood into the pulmonary artery. Venesection is said to be bad practice in such a case because the patient is already anæmic and lacking in strength. If we bleed we render them still more anæmic, but if we do not bleed the right heart will almost certainly become so distended as soon to cease its efforts to contract. When we are limited to a choice of two evils in other matters we instinctively choose the less; why not in this case? I have for several years advised and practised venesection in all cases showing this symptom-group; always with some relief at least, and, in a large proportion of instances, with recovery if the bleeding has been done before the right heart has been too greatly distended. If a full stream of blood can be obtained, 6 to 10 ounces will suffice; but if the stream is small and trickling, little good will result because the tension will not be lowered quickly enough to permit prompt contraction of auricle and ventricle. If relief can be obtained by a small bleeding taken in a gushing stream, the venesection may be repeated in thirty-six to forty-eight hours if deemed necessary. In the syncopal type venesection is uncalled for, as the heart is not laboring with an excess of blood. *Oxygen* by inhalation has been highly recommended by many for the relief of dyspnœa; my own experience with this agent has not been very satisfactory. A very able physiologist tells me that fresh air contains as much oxygen as can be absorbed into the blood. However, oxygen is highly spoken of by good observers, and has been reported as especially effective if passed through absolute alcohol in a wash bottle. Given in this way to animals showing heart failure from an overdose of chloroform it is reported to have had very marked effect.

*Hydrotherapy.*—Hyperpyrexia is fortunately not of frequent occurrence in pneumonia, so that resort to general hydrotherapy is not often called for, especially in the adult, for whom it necessitates too much disturbance, where rest is of such importance. For children to whom the bath can be given easily it often proves of great use in reducing unduly high temperature, stimulating circulation and respiration, quieting restlessness and delirium, and inducing sleep. The temperature of the water should not be much below 90° F. For the adult, cold sponging usually serves to quiet restlessness and give sleep in mild cases, especially if they are in fresh cool air. Much importance is attached to the use of cold compresses to the chest, their effect being attributed to the stimulation of the circulation in the skin, thus aiding the general circulation; and, in the second place, to stimulation of the vasomotor nerves of the pulmonary vessels. Opinions, however, vary as to the existence of pulmonary vasomotor nerves. Some of the ablest experimental physiologists point out that if there is a vasomotor nerve supply to the pulmonary vessels it must be very feeble, as it is undemonstrable. And further, they say that their existence cannot only serve no good purpose but would prove a positive danger, as if stimulated so as to cause spasm by any cause at any time there would be dangerous embarrassment of the pulmonary circulation. Cold compresses doubtless prove useful in some cases, especially if they cause deeper respiration, but their frequent changing is irksome and may fatigue

the patient. Is it not possible that their effect is largely psychical, especially to the physician, just as poulticing has been in former times?

## DISCUSSION.

*Dr. Oliver T. Osborne*, New Haven, Conn., agreed with the views expressed in the foregoing paper, particularly with regard to the importance of giving plenty of fresh air. The oxygen tank is useless; what is needed is an abundance of fresh air. The moment that this is furnished the temperature is likely to go down, the nervousness and restlessness to diminish, and the whole circulation to be improved. Also, anything which increases the activity of the skin, such as proper bed-clothing, sponging, etc., tends to cause the kidneys to act better, to diminish the cerebral and pulmonary congestion, and to bring about a general improvement in the patient's condition. A little solid food like cereal is much better than milk alone. Anything which tends to produce gastric irritation or tympanites is the worst thing that can be given. He agreed with Dr. McPhedran that nothing is more valuable in the treatment of some cases than morphine. As to stimulants, nitroglycerin is often valuable, alcohol sometimes. Strychnine is administered too often in pneumonia, while digitalis rarely does good, but on the other hand is capable of doing serious injury by overworking an already fagged heart, and may also interfere with the proper action of the kidneys. He commended venesection in selected cases.

*Dr. J. N. Hall*, Denver, Colo., said that it is not likely that we shall ever be able to reduce the mortality from pneumonia, as we have that from some other diseases, like scarlet fever, diphtheria, etc. Persons suffering from these diseases are usually in good physical condition when they are taken down, whereas pneumonia patients are often physically unsound when they are attacked. In many of the cases the heart, kidneys or other organs have suffered serious injury as the result of some primary disease before pneumonia appears as a complication or sequel. People are most liable to be attacked by pneumonia when the vitality is low, and this fact tends materially to increase the liability to a fatal termination. Furthermore, a large proportion of pneumonia patients are well along in years when they are taken down with the disease. Pneumonia is often the last puff of wind which blows the senile patient away. When we consider these two points alone, it seems probable that the mortality from this disease will always remain comparatively high.

*The President, Dr. Wilson*, said that the clinical picture of croupous pneumonia is a diverse one. In each case it is made up of two factors in varying degree, the pulmonary lesion and general toxæmia. Accordingly, when we talk of pneumonia we are speaking of an affection which manifests itself in different patients in many different ways, and this point should be borne in mind when we consider any of the various aspects of the disease. The bacteriologists had worked over the problem of a rational treatment for pneumonia for years, and he expressed the hope that some of us might live to see the dawn of a successful method with bacterial serum. At present, however, we have no specific for the disease and an expectant, symptomatic plan appears to give the best results in the large majority of cases. He agreed with the previous speakers as to the importance of hygiene in the management of pneumonia—plenty of fresh air, an abundance of water, a limited diet, and certain drugs, like the laxatives. He also agreed heartily with Dr. McPhedran as to the value of opium in some cases. Dover's powder, or even morphine hypodermically, can be given in certain cases not only without danger but even with marked benefit to the patient. As already stated, we know of no specific for pneumonia. Quinine, creosote and other drugs which have been lauded as cures for the disease have, after adequate trial by skilled clinicians, been laid aside. Some of the patients get well without anything but expectant treatment. Others die in spite of the most careful and skillful management and treatment. He cited the case of a young man with an extensive pneumonia of the left lung who appeared to be doing very well in almost every way. In examining him, however, he

noticed that he became cyanotic whenever he was turned upon his side. He called the attention of the attending physician to this symptom and gave a bad prognosis. The patient died, although for a time there seemed to be every reason to believe that he would get well. That fresh air is an important factor in the management of pneumonia is borne out by statistics from field hospitals in military campaigns. We should not forget, however, that the men who go to these hospitals are picked men physically. At any rate, a large proportion of them recover, and this fact has strengthened our belief in the value of the fresh-air treatment. An initial large dose of quinine, calomel in the form of Dover's powder, plenty of fresh air, and abundance of water, quietude (no frequent examinations by the physician to disturb the patient)—these, in the main, give the average pneumonia patient the best chance.

*Dr. Alexander D. Blackader*, Montreal, said that several years ago interesting experiments were made by Romberg and Osler to determine the exact cause of death in the infectious diseases. They showed that death was due, not so much to the abnormal condition of the heart muscle, as to diminished blood-pressure throughout the body, as a result of which the patient was bled into his own veins. In pneumonia we have not only the toxæmia, but also the consolidation of the lung and a tendency to lowered blood-pressure, and an abundance of fresh air is of great value in combating these conditions. Experiments have recently been reported which go to show that the exposure of the body to a current of cold air causes a general rise of arterial pressure, while warm air produces a fall of blood-pressure. Others have shown that through action on the nasal mucosa, as by cold, a marked rise of blood-pressure can be produced, the vasomotor stimulation being greater than that which can be brought about by the use of drugs. Thus, in supplying pneumonia patients with an abundance of cold fresh air we have a measure which serves not only to counteract to a considerable degree the depressing effects of the toxins on the vasomotor centers, but also to keep up a constant and even stimulation which, acting throughout the disease, does great good. Warm fresh air does not appear to be equally beneficial. Venesection is usually performed too late, and, as a result, the clinician fails to secure the good effects which often come from bleeding earlier in the disease.

*Dr. D. Olin Leech*, Washington, D. C., said that he treated pneumonia on the assumption that there is no specific for the disease, depending mainly upon fresh air, ice-bag to the chest, cold sponging, and a simple expectorant mixture. In some cases he gives codeine freely, and has had no bad effects from its use. In his hospital work he instructs the internes not to give nitroglycerin or strychnine or any other stimulant until their use is clearly indicated; nor does he give alcohol except in rare instances. He believes strongly in the value of fresh air in these cases. They need all the oxygen they can get and the best is that contained in fresh air. The ice-bag is useful in allaying pain and fever and as a stimulant to the circulation. Under this treatment he had lost no cases of pneumonia in his private practice during the past Winter. One patient died in his hospital cases, but that was an alcoholic with a bad heart.

# MALARIAL INFECTIONS IN THE CANAL ZONE AND THEIR TREATMENT.

By F. M. SHOOK, M.D.,

P. A. Surgeon U. S. N.; Lecturer on Tropical Medicine in Jefferson Medical College, Philadelphia, and Georgetown Medical College, Washington, D. C.,

WASHINGTON, D. C.

In this intensely infected focus of tropical malarial fever the most important malarial infection, from the standpoint of diagnosis and prognosis, is the estivo-autumnal, or to use the abbreviated nomenclature in common use on the Isthmus, the EA infections. Single tertian and double tertian infections are very common, and they comprise 50 per cent. of the infections at certain times of the year. They present no material differences in clinical symptoms from the tertian infections in the States, and they yield readily to quinine, when given in a form that is easily absorbed. Quartan infections are very rare, and clinical charts showing quartan fever curves are practically unknown. Occasional blood-spreads show parasites which resemble quartan parasites very closely, and a series of spreads were sent up from Colon this Winter which were undoubted quartans. The principal types of EA infections on the Isthmus may be classified as follows:—

1. *Mild Infections.*—The attack may be preceded by several days of malaise, with headache, backache, insomnia, loss of appetite, the usual prodromal symptoms of nearly all infections; or it may come on suddenly after hard work, exposure, a drinking bout, or after any condition that would lower the individual's resistance. On admission to the hospital the temperature is around 103°, there is considerable prostration (a characteristic of EA infections), and severe headache and backache. Physical examination of a patient with a mild infection such as this is negative, with the exception of some splenic tenderness on deep pressure and in about 50 per cent. of cases a palpable spleen. Blood examination will show an EA parasite to every half-dozen oil-immersion fields. A mild case such as this is given 3 grains of calomel on admission, with 20 grains of quinine. The quinine is given in solution or in capsules. The quinine tablets on the market are viewed with considerable suspicion, for it is not at all an unusual occurrence for them to pass through the intestinal tract intact. The calomel is followed by salts the next morning and 10 grains of quinine are given three times a day. An ice-cap usually relieves the headache. The temperature falls by lysis and reaches the normal the third or fourth day after admission, appetite returns and the patient recovers his strength rapidly. After a week's treatment with quinine, 10 grains three times a day, the dosage is cut down to 5 or 10 grains per day. On discharge from the hospital he is advised to take 10 or 15 grains of quinine once a week for a few weeks.

2. *The Severe EA Infections.*—In this type of EA infections there is a high temperature, 104° or 105°, respirations are increased, the pulse follows the temperature, and there is marked icterus, very severe headache and pain in the loins, constant retching and vomiting, and great prostration. The physical findings of these cases differ from those of the foregoing. Over the bases of the lungs there is usually impaired resonance with râles on expiration and inspiration, due to the intense pulmonary congestion and œdema. The spleen is enlarged, palpable, and very sensitive. Blood examination will show from 5 to 10 EA parasites in every oil-immersion field of the microscope. However, these patients have often taken quinine to ward off an attack, and there may be no parasites in the peripheral circulation on that account. Clinically, these cases resemble pneumonia, and one of the commonest errors in diagnosis is to mistake severe EA infections for this disease, and *vice versâ.* Malarial fever and pneumonia may both be present in the same individual, neither one affecting the other. A leucocyte count will probably differentiate the two, though some cases of pneumonia have a low leucocyte count; so that it is not at all unusual for a diagnosis to remain in doubt for several days. A differential leucocyte count will sometimes give a clew to a differential diagnosis in these doubtful cases. In these severe infections no time must be lost in getting the patient cinchonized. On account of the nausea and vomiting it is impossible to give quinine by the mouth, and the drug must therefore be given hypodermically. In giving quinine hypodermically the buttock is first selected for the injection. The skin is made surgically clean, and the needle and syringe are boiled, but not the quinine solution. The needle is plunged deeply into the muscle at right angles to the skin and the solution injected slowly. The puncture wound is closed with a few drops of collodion. An abscess following a quinine hypodermic injection is a very rare occurrence if this technique is followed. These severe EA infections get 15 grains of quinine hypodermically every four hours until 75 grains have been given, or until the vomiting has ceased. Sometimes after the first or second hypodermic the vomiting ceases and all the symptoms are alleviated. If this occurs, the injections are discontinued, and 10 grains of quinine in solution or capsule are given t. i. d. The temperature chart of one of these severe infections often simulates the chart of a pneumonia exactly, and also the temperature often falls by crisis. If it falls by lysis the curve is longer than in the milder EA infections and reaches the normal on the fifth or sixth day, instead of the third or fourth. After these severe infections quinine is given for several weeks. In the cases where it is discontinued a relapse usually follows, which may be as severe as the original attack. Convalescents from such attacks are sent over to Taboga Island, where with good food and rest they rapidly recover strength.

3. *The Mixed Infections.*—Infections with both T and EA are very common. The subjective symptoms are identical with these of an EA infection, but the temperature curves present many anomalies. The treatment follows the same general rule, viz., if there are any pernicious symptoms present, such as extreme prostration, hyperpyrexia, nausea and vomiting, 15

grain hypodermics of quinine are given every four hours for five times, or until the pernicious symptoms have abated. The physical examination of a case with mixed or double infections gives the same picture as that of a single infection, and the convalescence and after-treatment present no unusual features.

4. *The Pernicious Malarial Fevers.*—(*a*) The comatose type of malarial infection is the most common one in the pernicious fevers. The coma may vary from a deep one in which there is no response, to a semi-comatose condition in which answers to simple questions may be elicited. The temperature curves of these comatose cases follow no rule. They may vary from subnormal to a temperature of 103° or 104°, with occasional remissions. If the infection is the quotidian form of the EA parasite, the temperature is an intermittent one, rising usually in the afternoon to 104° or 105°. The quotidian infections are highly malignant.

(*b*) The hyperpyretic type is another of the common types of pernicious malarial fever on the Isthmus. Occasionally, in a patient apparently not very ill, the temperature rises to 102°, 103°, 104°, etc., up to 108° and 109°. Rectal temperatures at death may be as high as 110°. On account of the effect upon the brain there may be wild delirium or perhaps coma. Ocular symptoms, such as conjugate deviation and pupillary dilatation, are not uncommon. Blood examination shows from 15 to 20 EA parasites in the oil-immersion field. There is a generalized icterus, but the color is a shade different from the ordinary biliary jaundice. The spleen is enlarged, and pressure on the splenic area will cause the patient to flinch. The liver is occasionally enlarged, reaching to one or two fingers' breadth below the costal margin. The treatment of these infections is very unsatisfactory, and quinine, either hypodermically or intravenously, does not seem to stay the sporulation of the parasites. The majority of physicians on the Isthmus have discontinued the intravenous method of administration, and such pernicious cases receive quinine hypodermics; starting with a dose of 15 or 20 grains, which is followed by 15-grain doses every four hours. In autopsies on fatal cases the most striking features are the intense congestion and œdema of the lungs and the changes in the spleen. The latter is so softened that it does not retain its shape when laid on the autopsy table, and the pulp is dark and very friable. In the fatal malarial infections of cerebral type the brain shows surprisingly few gross changes. There may be a darkening of the cut surface, which may show minute capillary hemorrhages, but the paucity of gross changes is very striking. Smears from the spleen, bone-marrow and brain show countless sporulating parasites, provided the smears are taken within twenty-four hours after death. More parasites are apt to be contained in the gray matter of the cerebellum than any other part of the brain.

*Malarial Fever and Pregnancy.*—In cases of severe malarial fever in pregnant women there is added to the symptom-complex another element of danger. If large doses of quinine are given to control the attack of fever miscarriage will take place in 100 per cent. of cases, while if the dosage of quinine is small there is the danger of pernicious symptoms developing and

the case being rapidly carried to a fatal termination with a force that no amount of quinine can overcome. The safest rule to follow is to disregard the fœtus and treat the malarial infection as if pregnancy were not present. Very rarely, with the aid of complete rest and small repeated doses of morphine or codeine, miscarriage may be prevented, but miscarriage is the expected event. It is easily handled when it takes place, and does not lengthen the time of illness or influence its course unfavorably.

*Malarial Parasites in the Fœtus.*—The writer has been unable to find in the literature an undoubted case in pernicious malarial fever in which the malarial parasites were found in the fœtus. Dr. Norman E. Williamson, of the Isthmian Canal Commission Medical Corps, and the writer examined five fœtuses from pernicious cases. In the mothers, smears from the blood, bone-marrow, spleen, brain and placenta showed myriads of sporulating EA parasites, but careful examination of the blood and of all the organs of the fœtuses failed to demonstrate malarial parasites.

*Malarial Fever and Surgical Operations.*—The shock of a surgical operation often brings out a latent malarial infection, which occasionally is pernicious. In surgical cases in which the patient can be kept at the hospital for a few days prior to the operation a prophylactic course of quinine is given, 10 grains three times a day. In acute traumatic surgery it is customary to start 10-grain doses of quinine t. i. d. as soon after the operation as possible. If the prophylactic administration of quinine is neglected a very severe and occasionally a fatal attack of malarial fever will follow the operation.

*Malarial Fever in Children.*—Children stand the effects of a malarial infection better than adults, and it is not unusual to admit a mother and her child to a hospital ward, both patients showing the same number of parasites in the blood examination, but with the mother desperately ill and the child only slightly so. Children are often brought in suffering from chronic malarial infection, with anæmia and tender and enlarged spleens. Pernicious malaria when it does occur in children not infrequently simulates cerebrospinal fever, and the autopsies show the cerebral capillaries filled with sporulating parasites. In treating the severe infections in children 5-grain hypodermics of quinine are given instead of 10 or 15 grains, and quinine carbonic ester, 5 grains t. i. d., instead of the quinine solution.

## SUMMARY.

Experience of physicians on the Isthmus emphasizes the following points:—

1. In tropical malaria quinine should be given either in solution or capsules, as there is danger of the non-absorption of tablets.

2. If properly given, hypodermics of quinine rarely cause abscesses.

3. Quinine will not stay the fatal termination of some types of malarial infection.

4. For treating cases of malarial fever in adults in the tropics which do not show pernicious symptoms an initial dosage of 20 grains of quinine, preferably in solution, followed by 10 grains three times a day, has stood a satisfactory test in thousands of cases.

5. In the treatment of malarial fever in pregnant women in the tropics the safest rule is to disregard the pregnancy and treat the malarial fever in the usual manner.

6. After surgical operations in malarial districts in the tropics pernicious malarial fever may develop unless a prophylactic course of quinine is given prior to the operation.

7. In an examination of five fœtuses from cases of pernicious malaria neither malarial parasites nor pigment were found.

## DISCUSSION.

In reply to an inquiry from Dr. Barton as to what preparation of quinine he used hypodermically, Dr. Shook stated that he used the double hydrochloride when it was available; otherwise, an acid solution of the sulphate. The most important point in the paper appeared to him to be the advisability of giving quinine in the tropics before major operations to prevent the subsequent quick development of malarial symptoms: in other words, to prevent a latent form of malaria from suddenly becoming active. Such a manifestation was not infrequently observed after operations when quinine had not been administered previously, and the attacks sometimes proved rapidly fatal. The second point that he wished to emphasize was the advisability of leaving the fœtus out of consideration in treating pernicious malarial fever in pregnant women.

# IMPORTANT THERAPEUTIC INDICATIONS IN THE TREATMENT OF TYPHOID FEVER.

By J. BLAKE WHITE, M.D.,

NEW YORK.

He knew of no means to assure an early diagnosis which could as yet supersede an astuteness in discernment acquired by a very careful and intelligent clinical study and observation of a number of cases. The various laboratory tests were well enough to look to for confirming a diagnosis, but none of them, or all combined, could take the place of intelligent clinical observation at an early period of the disease. While awaiting the results of such tests valuable time was often lost, and even after this delay one might perhaps be led to incorrect conclusions by the return of a negative report. Then, long after the diagnosis should have been made, and suitable treatment instituted, positive results might be obtained. He would, therefore, rather rely on clinical evidences, backed by his own judgment and experience, than wait for confirmation by these laboratory tests.

That typhoid fever was due to a specific germ, which spent its virulence in the intestinal tract, was generally accepted. A pathological condition was thus produced from which most if not all of the succeeding serious symptoms arose, demanding our most energetic and zealous attention to combat. To the extent, therefore, that we succeeded in modifying the intestinal morbific process would we not only lessen the thermic changes attending the disease, but also prevent the various complications which were formerly so commonly met with. Having referred to perforation and its consequent peritonitis, pneumonia, meteorism and meningeal complications, he said that intestinal hæmorrhage now so seldom occurred that he mentioned it only to say that if it should make its appearance it could be readily controlled by the administration of five or ten minims of rectified spirits of turpentine, in a soft capsule, at its earliest manifestation, and repeated at intervals of from two to four hours. Thrombosis and embolism were sequelæ to be expected occasionally, but by judicious attention to nutrition throughout the course of the disease, so as to maintain the blood in as good condition as possible, these might generally be averted. At an early stage—about the second week, when, under the antiseptic treatment employed by him, the temperature, with rare exceptions, declined to or near the normal—he usually gave some alcoholic stimulant, in addition to strychnine, believing that by this means convalescence was apt to be rendered more rapid and satisfactory.

The Brand bath or any other process of tubbing was in many instances too exhausting to be of benefit, and in some cases was positively harmful. The custom of applying chilling hydropathic treatment as a routine procedure could not, therefore, be too strongly condemned. His own observation of this means

of reducing the temperature had satisfied him that it was the most irrational method of treatment that could be devised, since it was not expected to have, and never could have, any effect upon the pathological cause of the temperature, the combating of which was, after all, the chief indication for treatment. He was willing to admit that ablution had some useful application in developing vital activity and strengthening the power of resistance in the system; therefore he approved of and practised regular lavations with sterile water and alcohol, but he always directed that the water should be tempered to the enduring capacity of the patient. He used lavages more as a hygiene measure than for the purpose of merely effecting a reduction of temperature; believing that this could be more rapidly and permanently lowered by medication directed toward the modification of the morbific processes in the intestines which were considered primarily responsible for the fever.

It was of vital importance that regular function of the bowels should be maintained throughout the disease and convalescence, but diarrhœa occurring at any time and threatening to become an urgent symptom should be controlled by appropriate remedies. Under the method of intestinal antiseptics, however, it was much oftener necessary to have recourse to means for relieving constipation, and for this purpose laxatives, enemata, or irrigation of the rectum with mild warm saline solution through a Kemp tube might be employed. Prior to 1896 the practice of antiseptic intestinal medication was brought to the attention of the medical profession by Dr. Woodbridge, of Cleveland, though his method of treatment did not receive the consideration which it deserved. Clinical experience of accomplished and competent observers, however, had tended to prove that antiseptic remedies of the group in which guaiacol occupied the first place, administered in the manner advised by Woodbridge, do lessen the condition of the bowel. The ideal treatment of typhoid fever, then, was that which, at as little expense as possible to the patient's vitality, has for its object the reinforcement of the natural powers, thereby affording a natural barrier to the inroads of the disease; to neutralize, if not destroy, and eliminate as far as possible the causes of morbific action before the products of germ infection have so far been established in the system as to materially impair the vital powers. For the causes of the fever, the toxæmia from local lesions, and the general blood dyscrasia, there was no better therapeutic resource than antiseptic medication. As a result of this method of treatment, Dr. White had found no affection so easily manageable as typhoid fever. He advised that as soon as the diagnosis of typhoid was made, or sooner, if there was any doubt about the matter, the antiseptic combination used by Woodbridge should be given, though in somewhat larger doses than he recommended. The best manner of administering the remedies was in tablet triturates, made friable enough to insure absorption, which should be taken at the rate of from twenty to thirty in the twenty-four hours; each tablet to be swallowed by two or three swallows of some pure spring water, unaërated. After some modification of the fever was obtained, usually by the end of the first week, he gave larger doses of the antiseptic, one tablet to be taken every three or four hours, with large draughts of water. Should a case not be seen

until the disease had advanced so far that internal medication was impossible, he gave sodium sulphoborate by hypodermic injection at intervals of two, three or four hours, according to circumstances, until the patient was able to take the antiseptic tablets by the mouth.

As to the dietary, he gave eggs, meat broths, and milk, and as soon as the fever lessened, generally in seven days or less, he allowed the patient to chew pieces of rare steak, without swallowing the meat, until such time as the digestive organs manifested an ability to dispose of solid food. Cereals, well boiled, were permitted at any time, and the resort to solid nourishment just as soon as the patient's condition warranted it, usually at the end of the second week. In concluding he dwelt for a moment on how much the successful management of a case of typhoid depended on the intelligence, fidelity and watchfulness of the nurse.

# THE TREATMENT OF LEUKAEMIA BY THE ROENTGEN RAY.

By REYNOLD WEBB WILCOX, M.D., LL.D.,
Formerly Professor of Medicine at the New York Post-Graduate Medical School and Hospital; Consulting Physician to St. Mark's Hospital,
NEW YORK.

THE following instance of this disease is presented because of the difference in type based on clinical as distinguished from purely laboratory conclusions, the considerable period of observation, and the fairly constant therapeutic results which it illustrates.

The patient is a medical student, Russian, 29 years old. His father died at the age of 43 from meningitis. His mother, now 55 years old, suffered from pain beneath and in her heart, and from shortness of breath for about a year, some twenty-seven years ago. The diagnosis was enlargement of the spleen. For the past seventeen years she has suffered severely from rheumatism. His two sisters are alive and in good health.

In Russia the patient held a government position necessitating absolutely indoor work, with a lack of exercise. For ten years he had been pale, but the most noticeable symptom was shortness of breath, commencing eight years ago and lasting about two years. When he arrived in this country, in April, 1906, he considered that he was well. After a brief stay in Connecticut, where he did translating, he went to Kentucky, working for his uncle in an ice-house and meat market for two years. The work was hard, the hours were long, and he complained of cruel treatment. During this time he complained of constipation and fever, but no chills, and was treated by a physician with calomel and quinine, the town having a reputation for malaria. About June, 1908, he felt pain below the shoulder-blade on the left side, and noticed a return of the short breathing; these symptoms disappeared after three weeks. From September, 1908, to June, 1909, he studied medicine in Boston. In the latter month a physician informed him that he was suffering from open hæmorrhoids, which accounted for the occasional bloody stools of the past eight or ten years. In August, 1909, the pain in the side and short breathing returned and he felt weak and thirsty. On September 24, 1909, he came under my observation. His pallor of skin and mucous membranes was profound. His pulse was 122, compressible, regular and weak. The heart boundaries and sounds were normal; Jaccoud's sign was absent. There was a marked *bruit de diable*. His respiration was 26, shallow, but without signs of dyspnœa. The liver extended to about two fingers' breadth below the free border of the ribs. The spleen occupied the whole of the left abdominal cavity, resting upon the pubes; on the right two fingers' breadth to the right of the umbilicus. It was hard, not sensitive to pressure and laterally slightly movable; the hilum was easily felt. There was no tenderness over the flat bones. No enlarged glands were felt. Although the patient appeared anasarcous, there was nowhere pitting on pressure. Nothing of note was found in the urine.

The following is the record of blood-counts, including the differential leucocyte percentage:—

| Date. | Hæmoglobin Percentage. | Erythrocytes. | Leucocytes. | Lymphocytes. | Polynucleears. | Myelocytes. | Eosinophiles. | Remarks. |
|---|---|---|---|---|---|---|---|---|
| 1909 | | | | | | | | |
| Sept. 24 | 62 | 3,200,000 | 500,000 | | | 50 | | Reported by patient from memory. |
| Sept. 27 | 72 | 4,000,000 | 212,000 | 17 | 40 | 41 | | Poikilocytosis quite marked; no malaria. |
| Oct. 12 | 72 | 400,000 | 117,000 | 21 | 24 | 17 | | Poikilocytosis not so marked. |
| Oct. 19 | 80 | 3,400,000 | 160,000 | 12 | 20 | 10 | 9 | All blood-cells show granular degeneration. |
| Oct. 27 | 76 | 3,600,000 | 190,000 | 28 | 18 | 9 | 11 | Granular degeneration not so marked. |
| Dec. 1 | 74 | 4,000,000 | 160,000 | 26 | 16 | 6 | | Poikilocytosis not so marked. |
| 1910 | | | | | | | | |
| Jan. 12 | 78 | 4,100,000 | 150,000 | 22 | 10 | | | Slight poikilocytosis. |
| Feb. 22 | 75 | 4,300,000 | 160,000 | 15 | 10 | | | No granular degeneration. |
| Mch. 10 | 92 | 5,400,000 | 150,000 | 14 | 7.3 | | 1.3 | |
| Apr. 29 | 98 | 5,200,000 | 71,000 | 6 | 8 | 9 | 3 | Very slight poikilocytosis. |

These blood-counts have been made by eight different microscopists, and in a general way those made on the same day agree with each other. It is regretted that one observer could not have carried on the investigation, in order that the personal equation might have been eliminated and the results have been more comparative.

The urine never showed the excess of uric acid usually so characteristic of the disease. Nor, indeed, during the treatment by the Roentgen ray was there observed an excess of phosphates from diminution of leucocytosis, such as has been constant in all my other cases of leukæmia.

The treatment was primarily empirical, based on the use of the Roentgen ray, and was carried out under the direction of Professor Carl Beck, at first by him personally, and later by Doctor Eric Beck. A hard tube was used, fifteen minutes' exposure over the spleen, twice or thrice weekly. The care with which this was carried out is shown in that no untoward symptoms resulted until March 14, 1910, when a slight erythema appeared and lasted for ten days. The exposures were omitted altogether until the 27th, then directed upon the back until April 2d, and afterward continued as before. Iron was administered during the last two weeks in October and the first in November. At other times arsenic in gradually increasing doses, in the official liquor potassii arsenitis, was given until gastric symptoms supervened; at these times it was omitted for a week, to be commenced in the minimal dose. As the administration of some of the newer forms of arsenic has yielded rather irregular results in my hands, it was deemed best not to employ them. There seemed also to be a causal relation between the amount of arsenic and the quantity of blood passed by the bowel. Either stopping the arsenic would diminish the amount, but not check it entirely, or the administration of thirty grains of calcium chloride or citrate in two ounces of water at bedtime would cause the hæmorrhage to cease—generally two doses would be sufficient. The frequency of ulcerations

produced by lymphatic hyperplasia of the intestinal wall suggests caution in the use of arsenic.

In making a diagnosis between the recognized forms of leukæmia, (1) splenomedullary, (2) lymphatic, and (3) the mixed forms, there is much confusion in the literature, but, clinically, the picture is fairly clear. In this instance, the massive enlargement of the spleen, taken in connection with the absence of tenderness over any of the bones, and of any enlargement of the lymphatic glands, would indicate that this particular leukæmia was of the splenic type, or possibly of the splenomedullary (sometimes designated *myelogenous*) form. The differential leucocyte count would seem to indicate the latter. A hyperplasia may originate in any hæmapoietic tissue, spleen, bone, lymphatic glands or other site of lymphatic tissue, but generally one type predominates, especially in the more acute forms. In the slowly progressive types, there is more difficulty in determining where the disease originated. The more one studies the patients, the more he is inclined to believe that the disease is seldom strictly confined to one organ or set of organs; nor, on the other hand, is it ever as generalized as one might expect.

On April 28, 1910, the lower border of the spleen was but two finger-breadths below the free border of the ribs; its consistence was hard, owing, doubtless, to the hypertrophy of the connective tissue during the long period of its enlargement. The pulse was seventy-two, of good volume and tension. The respiration was twenty-two, without signs of dyspnœa. The pallor had largely disappeared, and for the preceding two weeks the patient had engaged in active employment.

What the final results of the Roentgen ray treatment will be, no one at present can state definitely. Six years of observation have led me to believe that in this type of leukemia, essentially splenic, reduction of the leucocytosis, betterment of the anæmia, improvement of the general health, is more rapidly and surely brought about by the skillful employment of the Roentgen ray than by any means which we had hitherto possessed. It is also believed that both iron and arsenic have still a place in the therapy of this disease. Under this treatment remissions are constant and intermissions generally pronounced. Relapses do occur, but they are more or less, generally more than less, amenable to the same treatment.

## DISCUSSION.

*Dr. Robert T. Morris*, New York, said that within two years he had had three cases of myelogenous leukæmia under observation extending over considerable periods. All three had distinctly improved under X-ray treatment. In one of the cases the diagnosis of sarcoma of the spleen had been made. The disease was far advanced, and the patient was weak, emaciated and failing rapidly. Apparently she had not long to live. She was given the X-ray treatment, and her condition progressively improved. She is now able to go out riding in an automobile, whereas at the beginning of treatment she could hardly turn over in bed.

*Dr. Wilcox* said he had reported the case because the patient had been under treatment for so many months. His experience had been that there is usually an early improvement, and then the patient passes from observation. He had watched this man, however, since September, and the blood-counts and other observations had been very carefully made. He hoped that other clinicians might have the same fortunate result in the treatment of this disease by the Roentgen ray. He would like to have an opportunity to observe one of these patients for years, instead of months, so that he might ascertain what the end results really are.

# HIGH FREQUENCY CURRENTS IN THE TREATMENT OF ARTERIOSCLEROSIS.

By THOMAS E. SATTERTHWAITE, M.D.,

NEW YORK.

His attention was first called to the beneficial effects of high frequency currents in 1901. He then had under his care a physician who was recovering from a mild cerebral hæmorrhage. From the first he had continuously the infrequent pulse, 30 to 40. In addition to treatment by various heart tonics, he was given a quite extensive course of electricity by Dr. E. B. Perry, and there was no doubt in Dr. Satterthwaite's mind that this was attended by both temporary and permanent benefit. Static electricity was employed, with long sparks and the fine needle spray. In another case, of mild arteriosclerosis with aortic disease and cardiac hypertrophy, in a married lady of 65, the Nauheim treatment was given, followed by a course of iodine, and subsequently she was treated with the high frequency current by Dr. W. W. Johns, of Utica, N. Y. Previous to her coming under the author's care the maximum pressure had been 200. When the electrical treatment was begun, on February 17, 1909, it had fallen to 185. On March 27th it was 165; on April 10th, 150, and on April 17th, 145. There was also marked improvement in her general condition.

The method he now recommends is as follows: The patient is first subjected for a few minutes to the light bath, by means of which the blood is brought to the surface, and a sedative effect produced. Then the static breeze may be given: The sliding poles are pulled apart, so that there will be no spark, and the negative side of the machine is connected with the insulated platform by the long brass shepherd's crook, while the positive pole is grounded. The metal standard being placed near, with the crown over the patient's head, the negative electricity streams over his face, so that he feels the breeze. There is also an odor of ozone, which fills the room, the oxygen of the air having been changed to ozone, or, in other words, electrified. This treatment, which is continued for from five to ten minutes, is very soothing and helpful in asthenia. The patient is then subjected to the high frequency current. The plant for this consists of a resonator combined with a d'Arsonval solenoid and adjustable spark gap and a pair of condensers of the Leyden jar type. This apparatus is operated by a static machine of sixteen plates. The patient reclines on a "condenser couch," which is insulated by means of glass feet. Its cushion has on its under surface a fine metal plate, which extends its entire length and is connected with one pole of the Oudin resonator. The other pole of the resonator is connected with a vacuum electrode, and the fluorescent spark discharge is applied through the clothing of the patient by the operator's slowly moving the electrode over the surface. The séance lasts from ten to fifteen minutes.

It is generally held that the static machine is more sedative and more efficient in other respects than the coil. The powerful waves of the static form of electricity cause short waves of vibration in the capillaries, which do no injury and promote metabolism in a remarkable manner. In Dr. Satterthwaite's experience, a diminution in arterial pressure is the regular sequel to the use of the high frequency current. The séances should not be prolonged beyond the time at which the pressure falls to normal, as this may prove harmful. Moutier has claimed, very properly, that while high frequency currents reduce arterial pressure, they cannot be said to be uniformly effective, as their action may be inhibited by errors of diet and other causes. Though as a rule he was able to secure a reduction in the pressure, in occasional instances this required as many as from sixteen to twenty sittings. The reduction once obtained, however, he claims, can be maintained for as much as three years without relapses. It has sometimes been advised to use the faradic current as an adjuvant. Intestinal atony is often a complication of arteriosclerosis, and here the faradic current, applied over the abdominal walls, may be helpful in relieving the constipation. In addition, Dr. Satterthwaite uses mercury, iodine, iron and arsenic, according to the indications present.

## DISCUSSION.

*Dr. P. Brynberg Porter*, New York, said that the case of the physician reported by Dr. Satterthwaite was a most interesting one. He had known the patient intimately, both before and during his illness. The man is now in remarkably good condition considering the nature of his trouble.

# FURTHER STUDY OF DIABETES AS AN INFECTIOUS DISEASE.

By ALFRED KING, M.D.,

PORTLAND, ME.

One year ago, at the meeting of the American Therapeutic Association held at New Haven, Conn., I ventured to express publicly the opinion that diabetes mellitus is an infectious disease, due to the presence in the blood of the yeast fungus, *saccharomyces cerevisiæ*. In support of this theory were presented the facts that this fungus is found in all diabetic urine; that I had obtained a pure culture of it from the blood of every case I had been able at that time to examine, sixteen in number; that the opsonic index or resisting power of each patient varied with the physical condition from .46 to above 1, or normal; that by the use of a vaccine this opsonic index was increased and all symptoms of diabetes relieved, and, also, that pathology confirmed the theory and showed nothing to oppose it. The only link which seemed wanting to the absolute establishment of the theory was the fact that I had not produced the disease in the lower animals by injecting the fungus; yet, even on this point, I was able to present the experiments of Leo, who had succeeded in producing glycosuria in dogs by the administration of fermented diabetic urine which contained no glucose. One year more has passed, and though I have not yet had the opportunity, in a somewhat busy life, to experiment on lower animals or complete my investigations, yet with considerable additional experience I have found nothing to disturb my confidence in the theory or my faith that it will be established.

The theory is based on the facts that this fungus exists in enormous quantities in the blood, and that it forms certain soluble ferments or enzymes, as invertase and sucrase, which by a catalytic action on those sugars taken in food or produced in the processes of digestion, and also on glycogen, convert them into glucose. This action takes place mainly in the portal blood and liver, and the glucose, formed much more rapidly than normal, enters the general circulation, increases the natural content above .2 per cent., and appears in the urine. It is practically the same as taking glucose by the mouth, as it is absorbed quickly and in quantity without the delay of any digestive process. The excessive quantity in the blood is naturally eliminated by the kidneys.

My work during the last year has been along lines similar to those reported a year ago. I have now examined forty patients, and have obtained a pure culture of the fungus from a drop of the blood of every one with one exception. This was in the case of a little boy three years of age, of a very nervous temperament. The attempt to sterilize and prick the finger was accompanied by such nervous disturbance and resistance on the part of the little fellow that it seemed wiser to desist. It was not worth while to obtain it by giving an anæsthetic. The fungus was present in his urine. In testing the urine for glucose I have used freshly prepared Fehling's solution. In determining the percentage I

have used Purdy's solution.[1] If the drops of urine are added immediately to the solution on boiling, the result is fairly accurate. If the solution is boiled very long the result will vary with the escape of the ammonia. After ⅛ per cent. is reached there is no certainty of result, as the same number of drops of normal urine will decolorize the solution. For acetone I have used Lange's method.[2] For diacetic acid I have used Gerhardt's test. One or more drops of the solution of perchloride of iron, added to the urine containing diacetic acid, produce a color varying from light garnet to nearly black. For testing for β-oxybutyric acid I have used the method of T. Stuart Hart,[3] which depends on the removal of the acetone and diacetic acid by boiling the urine and then forming acetone by oxidizing the β-oxybutyric acid with hydrogen peroxide. The reappearance of the acetone is determined by Lange's test.

At first I treated diabetic patients in my office, but soon found that it was impossible to keep run of the diet, the amount of fluid taken, or the quantity of urine passed; so that accurate observations as to the results of treatment could not be obtained. As my purpose has been to study the disease and the

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[1] Purdy's solution for determining the percentage of sugar is made as follows:

4.752 grammes of copper sulphate,
23.5 grammes potassium hydroxide,
350 c.c. ammonia, U. S. P.,
38 c.c. glycerin,
Water up to 1000 c.c.

Dissolve the copper and glycerin in 200 c.c. of water; dissolve the potassium hydroxide in 200 c.c. of water; mix these two solutions, and add the ammonia and then water to bring the total to 1000 c.c.

Bring 9 c.c. of the solution to boiling and add suspected urine one drop at a time. If one drop decolorizes the solution it shows ten per cent. sugar; if two drops decolorize, five per cent., etc. Urine showing more than one per cent. sugar should be diluted with water a known number of times—four, for example—and then tested as above; multiplying the result by the number of times the urine was diluted.

[2] Lange's test for acetone: To 10 c.c. of urine add two or three drops of glacial acetic acid; shake and add a few drops of a solution of sodium nitroprussiate; mix and overlay with 2 c.c. of concentrated ammonium hydroxide. If acetone is present a purplish-red ring will appear at the point of contact within a few minutes.

[3] Dr. T. Stuart Hart's method for testing for β-oxybutyric acid: To 20 c.c. of the suspected urine add 20 c.c. of water and a few drops of acetic acid, and boil until the volume is reduced to about 10 c.c. To this residue add water to the original volume (*i.e.*, until it measures 20 c.c.); put this into two test-tubes (B and C) of equal size, 10 c.c. in each test-tube; to one of the test-tubes (C) add 1 c.c. of hydrogen peroxide, warm gently for about one minute (do not boil), and then allow the fluid to cool. Add to each test-tube (B and C) one-half of 1 c.c. of glacial acetic acid and a few drops of a freshly prepared watery solution of sodium nitroprussiate and mix; overlay the solution in each test-tube with 2 c.c. of concentrated ammonium hydroxide; allow these to stand for four or five hours, and at the end of this time compare the two test-tubes. At the point of contact between the ammonia and the underlying fluid B will show no ring (or a faint brown ring if much creatinin is present); test-tube C, to which hydrogen peroxide was added, will show a purplish-red contact ring if β-oxybutyric acid was originally present; if β-oxybutyric acid was not present, the two test-tubes will not differ in appearance. If the two test-tubes are now shaken, the difference in color will be seen throughout the fluid; this difference is intensified by allowing the tubes to stand for fifteen or twenty minutes after shaking.

effects of treatment, I have for some time refused to treat any case unless the patient would go to a private hospital and be completely under my care for at least a month. In treating an infectious disease I believe that the whole physical condition of the patient should be considered; also the methods of treatment found beneficial in the past, even though greater knowledge be necessary to explain their value. To disdain former methods of treatment, "the good the past has had," and depend merely on rest, fresh air and diet is narrow, unscientific and unprogressive. The treatment of diabetes must be hygienic and medicinal. It must aim at removing and controlling the cause, as well as the injurious effects. Every effort made by nature to maintain the health of the body and overcome and protect the system from infectious germs and their effects should be assisted. Nature's efforts are frequently made known by the actual cravings of the patient, and should receive attention. One of the cravings of a diabetic is thirst. I believe it should be satisfied. The taking of fluids dilutes the glucose, acetone, diacetic acid, and -oxybutyric acid in the blood, relieves their irritating effects upon the vessel-walls and tissues, and facilitates their removal, as well as that of the germs from the blood. To blunt this sense of thirst by acids, opiates or other drugs, and to fail to satisfy it, will sooner or later do injury.

To regulate the diet of a diabetic is a most important part of scientific treatment and calls for much study and care. As sugars commonly taken in foods are speedily converted into glucose without the aid of any of the digestive processes except the invertin of the intestinal mucosa, as their omission can be supplied in another and better way, and as the little sweeting needed can easily be supplied by saccharin, I believe it is better to forbid any use of the sugars except what may be in a little cream or milk. Even milk should be limited to a small amount. It is true that large quantities of milk have been used with apparent benefit in some cases. A milk diet alone has been used with good results, but it contains 4.6 per cent. of sugar of milk, which is converted into glucose and galactose by the invertase, and while some of this may be consumed in the system, yet it is much more than the normal content of the blood. I have found it to increase the glycosuria. Again, casein is easily changed to glycogen, and cream may promote the formation of fatty acids. It is a fact that sugars aggravate the glycosuria and may promote the formation of the invertase. The digestive organs are of vast importance to a healthy body, aside from the secretion of digestive fluids. A diet composed of the end products of digestion would certainly be repulsive and, given alone, would lead to serious organic disturbances. The digestion of starchy foods is gradual and slow, and varies with the variety of food, and there is a slow introduction into the portal circulation of the maltose or glucose formed. Starchy foods promote the functional activity of the digestive organs and there is a craving for them, especially for bread, in the diabetic. I believe this demand of nature should be granted with limitations. It is known that the omission of all carbohydrates is followed in healthy persons by the appearance in the urine of acetone and diacetic acid and by an acidosis. It is also known that when these substances appear in a diabetic's urine the sudden withdrawal of all carbohydrates may be followed by a serious change,

possibly a fatal termination. Glucose is less injurious than the acidosis. Three ounces of starches per day prevent the acetone and diacetic acid. I believe in limiting the starchy foods in diabetics to not less than three ounces per day and in satisfying the craving of the patient so far as possible. I believe that blunting this desire by drugs is injurious, and to try to gratify the taste with an imitation food containing no starch is a senseless piece of deception unworthy of an intelligent physician. It seems like a revival of green glasses for horses to make them eat shavings. I do not believe in gluten foods. They do not satisfy, and they contain more or less starch, which can be given in a more palatable form and in equal quantity with less harm. Gluten foods are injurious. In one case the opsonic index of a patient living on gluten bread dropped from above normal to .46. Again, the limitation or omission of carbohydrate foods, which provide heat and energy, leads to loss of health, strength and weight. Such losses are too serious to be permitted. It is remarkable what abusive treatment some patients will stand, nor is it to be wondered at that many diabetics to-day, having escaped from the hands of well-meaning physicians, have found their health much improved by eating what they like. An unbalanced ration is unsatisfactory and injurious to man, as well as animals. I cannot agree with those who stop at once all carbohydrates on beginning treatment. Mild cases do not require it. In severe cases it is dangerous. Limiting patients to 1 ounce three times a day is sufficient for all practical purposes. The advisability of giving smaller quantities at shorter intervals is a matter for investigation. When this quantity is followed by much glycosuria it is well to reduce gradually the amount of proteids and watch the effect. So also in acidosis it is well to omit the fats likely to form the fatty acids. Of the carbohydrates I have used white bread, cornmeal, oatmeal, potatoes, beans, peas, nuts and bananas. The only sugar used is in a small portion of milk or cream.

In regard to drugs, I believe tonics like iron, arsenic, strychnine, quinine and hypophosphites, especially those invigorating the nervous system, are exceedingly valuable for relieving the existing weakness. Such laxatives as cascara, castor-oil, calomel and soda may be required. For acidosis, sodium bicarbonate should be given in half-dram doses every two, three or four hours. Antiseptics to retard the action and growth or to destroy the fungus have been found of no use. Creosote carbonate, one of the most effective in destroying the life of the fungus, carefully given in large doses, was tried on several cases, even to smoky urine, but produced no effect. There is no antiseptic which can act solely upon germs when in the tissues of the body; they must be combated by assisting natural efforts for immunization. The vaccine treatment stands alone as most effective. It restores the strength and sense of well-being, relieves the thirst, checks the polyuria, reduces the sugar content of the urine, and lessens the frequency of micturition. All this it does by increasing the resisting power and destroying the cause. The preparation of the vaccine and the method of administration have been changed from time to time. One year ago two patients on uncontrolled diet were having 6 to 8 per cent. of sugar in their urine. A vaccine made of fungus originally obtained from urine heated to 60° C. for an hour was used. This made them feel better and stronger, lessened the frequency

of micturition, and reduced the glucose to 5 per cent. Less than this it would not go. A vaccine from the fungus obtained from blood was used with a slightly better effect. Then five plate cultures were made, from fungus obtained from the blood of five different patients, to observe the comparative rapidity of growth. All varied, but some were much more rapid-growing than others. A vaccine was made from the most active-growing. The percentage in both cases now dropped to 2 per cent., where it remained for some time. Later the use of a sealed glass tube in sterilizing the vaccine showed it to be more effective, and the urine now contains from 1 to $^{1}/_{13}$ per cent. of sugar. These patients are not on a very restricted diet. The sterilizing of the vaccine requires temperature and length of time, varying with the age of the fungus. The higher the temperature and the longer the duration of exposure for making the vaccine, the less effective is the vaccine. The frequency of treatment is of importance. Twice a week soon brings the opsonic index above normal, but it is more effective than that. On watching the cases at the hospital it is not uncommon to have two cases running almost parallel. I have noticed that on the day following the use of the vaccine the quantity of urine would drop off from 4 to 20 ounces, and then come up again the following day. This change is more noticeable when the daily quantity is about 100 ounces. When the quantity is normal or below, there is slight if any variation, though I have seen it increase to normal. On changing to daily administration, I have seen two cases drop off 40 ounces in two days.

In reporting cases of diabetes it is difficult to classify them. We see mild and severe cases. We look with anxiety upon cases in young children, and even in young men and women, and we fear those having acetone, diacetic acid, and $\beta$-oxybutyric acid. We do not like to see the young with emaciation and the hectic flush. Yet these are not of the same class, for their condition may be caused by the omission of the carbohydrates, improper diet, acidosis, or tuberculosis or other wasting diseases. We have every reason to be encouraged when, with other improving symptoms, we find an improvement in color, flesh and strength.

Of the forty cases seen since I began my investigations, ten were simply examined. Two have died, both in the early months of my work. One was a little boy, and the case seemed a mild one. The fond father was a physician, and I have thought that the anxiety of the parent over the glycosuria led to such restrictions of diet that the resulting acidosis occasioned the fatal termination.

The other death came with coma. The patient was a young woman with intense acidosis. There was profound anæmia, shortness of breath, loss of strength and flesh. I think change of diet had to do with her death, and had it been possible for her to have the care, diet and treatment to be obtained now in a hospital I believe the fatal termination would have been warded off. Twelve patients received office treatment only. Two of these I saw so few times as to be able to make no observations worthy of note. One lived in the country and has improved very much, but it was difficult to provide proteids as she was situated, and in this way the treatment was unsatisfactory. Four were mild

cases. On vaccine treatment with a satisfying diet, and much more than 3 ounces of carbohydrates per day, they are conscious of no disease, are greatly improved in health. Their urine at times shows no sugar, at others a small fraction of 1 per cent.—⅛ to ⅛. One case, more severe, is greatly improved. He has but ½ per cent. of sugar, with no consciousness of disease. One case improves greatly under treatment, but when she begins to feel as well as ever she disappears to follow her own sweet will. Two of the most severe and chronic cases I have already referred to in connection with the preparation of the vaccine. With but little restriction of diet their health has improved very much during the past year, and, instead of 6 to 8 per cent. of sugar, they now have but 1 per cent., or a little under. The last of these office cases I will speak of later as one in which the treatment was begun early in the disease.

Hospital cases do much better than office patients. The mild cases show greater improvement in general health, can use a diet apparently unrestricted, and soon have less than ⅛ per cent. of sugar, or none at all. In cases of greater severity some results have been equally good. One case was treated at her home in the country. She was 56 years of age. One sister had died of diabetes at the age of 65, after an illness of nine years. There was no reason to suspect contagion in these two cases, as they lived far apart and did not see each other for thirty years, but each then had the disease. This patient had most decided reactions on the use of the vaccine. She, in fact, is the only patient who has shown any marked reaction. Its use the first time was followed by chill, fever and delirium that night. The dose had to be reduced, and the vaccine was made from a culture of her own blood. The first treatment stopped the polyuria and greatly reduced the percentage of sugar. She improved for a while, but as she lived in the country she could not get proper food. She developed an acidosis and began to lose flesh and strength, and the hectic flush appeared in her cheeks. She came to my hospital for treatment. Here the regular vaccine was used, but the quantity had to be reduced to one-half what the other patients were taking. On March 19th her urine contained 2 per cent. sugar and had a specific gravity of 1040, and acetone and diacetic acid, marked. Seven days later the specific gravity was 1030; sugar, ½ per cent. Five days later the specific gravity was 1018 and there was no sugar, though a trace of acetone and diacetic acid. No sugar was found during the remaining five days of her stay in the hospital, but there was still a trace of the acetone and diacetic acid. The quantity of urine was small, being only a little over 2 pints in twenty-four hours. While under this treatment she gained flesh, strength and a natural color and felt perfectly well. Another case was treated outside the hospital for a time with marked benefit. She became ill with a severe bronchitis, and her physician gave her cough mixtures with syrup. She recovered from this with great loss of health and I advised a month at the hospital. When I first saw her she was passing 9½ pints of water per day; sugar, 3 per cent.; specific gravity, 1035. The sugar was reduced by treatment to 1 per cent., with total quantity of urine also greatly reduced, and no consciousness of trouble. On entering the hospital, March 9, 1910, the daily quantity was 34 ounces; specific gravity, 1012; sugar, ⅔ per cent. On March 12th there was but ⅕ per cent. of sugar, on March 26th it had

wholly disappeared, and none was found during the remainder of her stay at the hospital. She also gained flesh and strength and felt perfectly well.

I have had at my hospital four young people about the age of twenty. On entering they were passing daily over 100 ounces of urine, which contained sugar, acetone, diacetic acid, and $\beta$-oxybutyric acid. These to my mind are serious cases. Under the use of vaccine they feel stronger and better and the sugar decreases, as also the other products mentioned. The day following the use of the vaccine there is usually a drop in quantity of from 4 to 20 ounces of urine. As I have said before, on observing this and changing to a daily use of the vaccine, in two cases the total quantity was reduced 40 ounces in forty-eight hours. These cases require at least six weeks' treatment to get the total quantity to remain below 4 pints and a duration of hospital treatment of several months to get best results. I have had in the hospital one little boy of three. He had been sick several weeks with loss of flesh, color and strength. His urine contained 1 per cent. of sugar, acetone and diacetic acid. Micturition was hourly. He remained at the hospital a month. Sugar was then ½ per cent.; acetone and diacetic acid, a trace of each; micturition normal. He was able to sleep all night and greatly improved in flesh, strength and color; in fact, was apparently well. In spite of a satisfying carbohydrate diet, he was passing but a dram of glucose in twenty-four hours. His condition to-day, after four months of treatment, three of which were at his home, is about the same, only there is no acetone or diacetic acid in his urine. He plays with other children and is apparently as well as any of them.

Cases of diabetes taken early give the quickest and best results. One case in point is a man aged 58. On September 1, 1909, his urine had specific gravity of 1045 and sugar 1⅑ per cent. He had been conscious of trouble but a few weeks. Thirty minims of vaccine were given and the diet restricted as to carbohydrates to one slice of bread or one potato with each meal. A pure culture of the fungus was obtained from a drop of blood. His opsonic index was 1.14. September 4th the specific gravity was 1035; sugar, 1⅑ per cent. September 10th the specific gravity was 1027; sugar, $^{1}\%_{17}$ per cent. The vaccine was given twice a week. On October 12th there was no sugar. Two attempts to get culture from blood were negative. He withdrew from treatment and I did not see him professionally until a week ago, an interval of some six months. He had been eating everything except sugar in coffee, going to dinners almost daily, had gained ten pounds, and was feeling as well as ever. His urine had been examined frequently without the finding of sugar. I found less than ⅙ per cent. of sugar at one examination, and three days later, after the partaking of a fine dinner the night before, his urine contained no sugar. A culture from the blood showed the fungus still lurking in his system. Another case was that of a man of 45, who came to the hospital March 23, 1910. Fungus present in blood; specific gravity of urine, 1035; sugar, 5/9 per cent. on restricted diet. He received vaccine every other day. On March 26th the sugar was 5/13 per cent. On March 31st none was found; on April 4th 1/7 per cent. sugar. For two weeks more none was found. Blood culture at end of that time was negative.

So I might report other cases showing the value of the vaccine treatment of diabetes. Those who see its effects now have no doubt as to its value. I am aware that much is still to be learned as to the preparation and use of vaccines for treatment of infectious diseases and in the study of immunization. I believe that Wright's work is epoch-making in the history of medicine. My own work on diabetes has given me increasing confidence in the truth of the theory and in securing still better results. The coming year offers still better opportunities for study. Mr. Drummond, who has been of great help to me in the work, graduates in medicine this summer and will be able to give still further assistance. This will enable me to work out some problems in regard to vaccine, to experiment on the lower animals, and to make still more careful observations. The work certainly seems more promising than a year ago, and I have great hope that it may prove of use in determining the cause and leading to a successful treatment of a somewhat obscure disease.

## DISCUSSION.

*Dr. N. P. Barnes*, Washington, D. C., said he thought that the work of Dr. King deserved special recognition from the Society. He therefore moved that a vote of thanks be extended to the author for his interesting and instructive paper. This motion, duly seconded, was carried unanimously.

*Dr. Howard Van Rensselaer*, Albany, N. Y., said that the results reported by Dr. King were different in some ways from those obtained by other observers. Under suitable conditions the yeast fungus destroys sugar, with the formation of alcohol. Now, if in diabetes there are present in the blood sugar and the yeast fungus, as suggested by Dr. King, he could not see why this action would not take place with the result that all of the sugar would eventually be used up and disappear from the blood, leaving the patient cured, though perhaps in a condition of chronic alcoholism. Thus the yeast fungus would be nature's cure, rather than the cause of the disease. He wondered whether Dr. King had not met with the same difficulty that he had encountered in the laboratory. He once found a germ in a place where it apparently did not belong, and he kept meeting it again and again in places where he least expected to find it. His suspicions were aroused, and he examined his stain and found that it contained great numbers of these germs.

*Dr. Osborne* said he had investigated three cases of diabetes in his laboratory, but had not been able to find the yeast fungus in the blood. Whether this was the result of faulty technique or not he did not know. He had been struck by the truth of Dr. King's observation that many diabetics do not begin to run down rapidly until they come under the physician's care. The only explanation which he could offer was that excessive dieting is responsible for this result. He believed that we are too much afraid of acidosis—not necessarily a diminution in the alkalinity of the blood, but the appearance of diacetic acid and acetone in the urine. According to his experience, this phenomenon does not always have the serious significance which is commonly attributed to it. In the course of strict dieting acidosis of a certain degree often occurred, and he frankly confessed that he had no liking for it; but he had found that in some cases if the dieting were kept up, and a certain point passed, the diacetic acid and acetone gradually diminished in the urine, and might ultimately disappear, even when the patient was on an absolutely starch-free diet. Since he had become convinced of this he felt safe in restricting the diet to a point which he formerly believed to be unjustifiable.

*Dr. T. E. Satterthwaite*, New York, asked Dr. King whether his proof involved cases in which the saccharomyces fungus, removed from the blood of patients suffering

from diabetes and introduced into the blood of the lower animals, had produced in them glycosuria. This subject was certainly a very interesting one. The theory, if sound, seemed to point the way to the use of vaccines in the treatment of glycosuria; but this seemed almost too good to be true.

*Dr. King*, in closing, expressed his appreciation of the kindly feeling of the Society. In reply to Dr. Satterthwaite's question he said that this had been done by Leo. The experiments were mentioned in Osler's Practice. As stated in the paper, he had not had an opportunity to conduct experiments of this kind, but hoped to be able to do so during the coming year. In reply to Dr. Van Rensselaer he said that whether or not the yeast fungus would act in the blood as it does elsewhere was an open question. He was inclined to doubt whether it would act the same inside the body as without. He discussed the question further, and offered a suggestion as to the manner in which the presence of the yeast fungus in the blood might give rise to glycosuria. By preventing coagulation by drawing off the blood into saline solutions he had been able invariably to get the germs, in spite of every antiseptic precaution which he could employ. His stain was an ordinary methylene-blue solution, and if it had been contaminated in the way suggested by Dr. Van Rensselaer all other specimens stained with the solution would have contained the germs. This was not the case. He had yet to meet with a case of diabetes in which he was unable to find the yeast fungus in the patient's blood.

# THE PREPARATION OF THYROID GLAND FOR USE.

By S. P. BEEBE, M.D.,
NEW YORK.

THE utility of thyroid extract in a variety of conditions had now been so thoroughly demonstrated that the demand for a standard preparation might no longer be ignored. The manufacturers at the present time supplied a variety of thyroid products prepared by different methods, and undoubtedly of differing therapeutic effects. During the last three years he had had many opportunities to compare the effects produced by various forms of thyroid preparations, and had arrived at the positive conclusion that the human thyroid extract, administered hypodermically, was by far the best for the human subject. In its effects upon simple goitre, myxœdema, cretinism, athyroid symptoms occasionally observed in late exophthalmic goitre, and various metabolic disorders associated with hypofunction of the thyroid, there was no other substance which acted so economically and efficiently as the proteid precipitated from extracts of normal human thyroid glands by acetic acid and heat at 44° C., and afterward thoroughly washed. Therefore, we should use only the proteid obtained by a similar method from animal glands. The prepared proteid showed quite as wide a variation in its iodine content as did the fresh glands, and before being used therapeutically it was essential that the proteid should be standardized on the basis of its iodine content, and a uniform intelligent dosage regulated thereby. For the standard, the proteid obtained from normal human thyroid glands had been selected. The average figures of a large number of iodine analyses of the proteid obtained from normal thyroid glands by the process mentioned showed that 1 gramme of the purified proteid contained 3.384 milligrammes of iodine. After the purified proteid from the animal glands was obtained, the iodine content was determined by the Riggs method, and, regardless of whether this proteid was richer or poorer in iodine than the standard, it was considered that each 3.384 milligrammes of iodine represented 1 gramme of the active thyroid proteid. For the purpose of administration the proteid was diluted with the appropriate amount of lactose, and made up into 2-grain tablets by the usual method. Tablets of different strengths were prepared, and 1, 2 and 5 per cent. tablets had been found to give a sufficiently wide variation in strength for all the usual requirements. By 1 per cent. tablet was meant that 1 per cent. of the dried weight of the tablet was made up of the purified thyroid proteid according to the standard described. It would be observed that, by this method of standardizing and preparing the proteid for therapeutic administration, a uniform physiological activity might be expected, regardless of the character of the glands from which the proteid had been obtained. For hypodermic use, solutions of the proteid in varying strengths, standardized on the iodine basis, had been put up in sealed glass tubes. The

products prepared according to the method referred to had now been employed for about two and a half years in a wide variety of conditions by a considerable number of experienced clinicians, and the results had demonstrated their value to such an extent that he had no hesitation in saying that this method of preparing and standardizing thyroid, giving as it did all of the physiologically active portions of the gland, with none of the toxic, deleterious substances contained in the whole extract, was superior to any method now in vogue.

DISCUSSION.

*Dr. Osborne* said that the method of assay described by Dr. Beebe appeared to be just the one we were looking for, and if it could be incorporated into the next Pharmacopœia we would undoubtedly be able to obtain pure thyroid preparations. As it is now we cannot depend on these preparations at all. Whether the various activities of the thyroid can ever be separated, chemically or otherwise, is a question for the future to determine. They could undoubtedly be utilized in the treatment of many diseases if they could only be differentiated. We speak of hyperthyroidism and hypothyroidism, but there are undoubtedly many activities of the gland which are not included under either of these terms and which may become deranged as the result of disease and produce symptoms, the true nature of which we do not now understand. At present we recognize hyperthyroidism and hypothyroidism according to the secretory activity of the gland as a whole, but, as a matter of fact, in either of these conditions there may be a disturbance of one or more of the individual activities of the gland; some may be acting too much and others too little, and if we were only able to differentiate them we should be in a better position to meet the symptoms which result.

*Dr. Satterthwaite* said we did not always obtain good results by treating exophthalmic goiter with thyroid preparations. Sometimes, however, the results were wonderful, and he cited a case in point. In another case in which he had every reason to expect a good result, he obtained none whatever. He believed that failure in these cases was often due to the use of a worthless thyroid extract; but, as a rule, his experience with this agent, both in exophthalmic goiter and myxœdema, had been most satisfactory.

*Dr. F. H. Gerrish*, Portland, Me., moved that a vote of thanks be extended to Dr. Beebe for his interesting and instructive paper. The motion, duly seconded, was carried unanimously.

*Dr. Morris* asked how it was that in cases of lack of development of the thyroid gland we obtained a beneficial result from the use of thyroids except upon the theory that we thereby supply a substance which is needed in the economy of the body, and which is lacking by reason of the imperfect development of the gland. He also inquired whether the enlargement of the thyroid in certain diseased conditions is a compensatory and desirable hypertrophy, brought about by the body in an effort to furnish an adequate quantity of thyroid secretion, or wholly a pathological condition. He saw many cases of goiter in his clinic, and they usually responded, more or less, to X-ray treatment. He had now a number of such cases under observation. One of his patients told him that she, with eight other girls, had become affected with exophthalmic goiter since drinking distilled water where they worked. He sent his assistant to investigate the matter, but he was unable to see the girls, because they had gone to other places of employment. He could not, therefore, verify the girl's statement as to the other eight, but she had no apparent reason for prevaricating, and was simply repeating a comment of the shop.

*Dr. Fisher* said he had used most of the various thyroid preparations upon the market, and had found that in a condition like myxœdema one of these preparations might give satisfactory results when another would produce no beneficial effects whatever. In the latter instance the failure was undoubtedly often due to the employment of an inferior or inert product. Unquestionably the thyroid preparations should be

standardized. The general results of treatment, however, show that there must be a goodly amount of thyroid in the average product. A certain proportion of cases of exophthalmic goiter respond to treatment by thyroid, and others do not. In the cases in which it does good the thyroid gland is undoubtedly in a condition of hyposecretion, possibly in an atrophic condition, as in some cases recently reported. When the preparation fails to produce any marked benefit, it would appear to be likely that the gland is in a state of hypersecretion. Much, however, remains to be learned about the various functions and activities of this gland.

*Dr. Beebe*, in closing, said that he had not intended by any means to assert that all or even the great majority of the thyroid preparations on the market are wanting in activity; but in his experience he had found a wide variation between the products of different firms and also between the different thyroid preparations of the same firm. Patients, also, differ widely as to the amount of thyroid they can take. There can be no question about the efficacy of thyroids in cretinism. In this disease the product seems to supply a need on the part of the system, and there seems to be no doubt that we can supply or make up for a number of the functions of the gland by giving thyroid preparations by the stomach; but, according to his experience, while many myxœdema patients improved under the treatment, they never became absolutely normal. He had used human thyroids in the treatment of three cases of cretinism, and found that much less of this product was needed to produce the desired results. He cited this as an interesting point, although he did not believe the method would ever be used to any considerable extent. While much good can be accomplished by the administration of the thyroids in exophthalmic goiter, much harm can also be done by their injudicious use. In reply to Dr. Morris's question as to whether the hypertrophy of the gland is evidence of an effort on the part of nature to supply a physiological need, he said that the question was a difficult one to answer. In some cases, where a reduction of the hypertrophy is brought about by the use of iodine, the diminution in the size of the gland is attended by the happiest results. In others, all the symptoms of overactivity of the gland continue, which would seem to show that, in some instances, at least, the hypertrophy is not a physiological process. The diseases of the thyroid are not simple affections, sharply defined one from another, but just as there are undoubtedly activities of the gland which we do not now understand, so there may be disturbances of function in addition to those which are recognized at the present time, namely, hypo- and hyper- secretion. Disease of the thyroid does not necessarily mean over- or under- activity; both may be present at the same time. The speaker urged a deeper study of thyroid conditions, and particularly a differentiation of the activities of the gland. In the face of the complex conditions which obtained in thyroid affections it was a mistake to generalize, as in simple diseases like typhoid, measles, etc. What is most needed is a classification of thyroid diseases.

# ASTHENIA UNIVERSALIS CONGENITA.

By CHARLES LYMAN GREENE, M.D.,
ST. PAUL, MINN.

To the acumen of Professor Stiller, of Buda-Pesth, we owe the identification and full description of this disease, which is congenital in foundation. Assuming with him that a large number of persons are born asthenic, and that this defect involves every structure and function of the body, one can readily follow his argument, which brings into one pathological circuit a multitude of ailments hitherto regarded and treated as separate and distinct conditions. Among these are the so-called phthisical habitus, neurasthenia of the commoner type, certain apparent renal inadequacies, functional albuminurias, nephroptosis, gastroptosis, enteroptosis and that enormously predominant group of dyspepsias known as the gastric neuroses. Stiller insists that an abnormally fluctuating or actually floating tenth rib is almost pathognomonic of this condition, and this the writer believes to be true, though to him the general structural stigmata are even more interesting.

These may be placed under several heads:—

(*a*) *Outward Signs.*—Small features; soft, fine skin; usually more or less pallid, loose-fitting and relaxed; slender figure, delicate bones; long thorax, narrowed or flattened, with sloping ribs, narrow epigastric angle, and the costal stigma described above. Upper and lower thoracic apertures and the pelvic inlet and outlet are said by Stiller to be narrowed. Active cases are generally more or less under weight.

(*b*) *Heart and Blood-vessels.*—Stiller emphasizes the fact that hypoplasia of both structures exists, and the writer believes that the fluoroscope will usually show a small, vertically placed, low-lying heart. Such hearts are easily strained and rendered irritable or temporarily incompetent by unwise exercise. It is generally true that asthenic individuals almost wholly escape degenerative diseases of the heart, blood-vessels and kidneys.

(*c*) *The Lungs.*—The lungs seem sluggish as regards expansion, and the areas of percussion resonance at the apices usually show a low maximum height, slight respiratory excursion, and, frequently, marked inequality between the two sides.

(*d*) *The Stomach.*—Gastroptosis will usually be found. Any of the multitude of gastric neuroses may be present and find expression in hyperchlorhydria, heterochylia, hypochlorhydria, achlorhydria or achylia.

(*e*) *The Intestines.*—Constipation is almost an invariable accompaniment of this disease. The writer has yet to encounter a case of mucous colitis in which the asthenic stigmata were absent.

(*f*) *The Blood.*—Active cases usually show some degree of anæmia.

(*g*) *The Kidneys.*—Serum-albuminuria in youth and childhood, without demonstrable renal lesions, is usually, if not always, associated with the

*asthenic habitus* and marked subnutrition. Rest and generous diet is the regimen for these cases. Practically all asthenic patients show a subnormal nitrogen excretion if any active symptoms of functional derangement are present.

(*h*) *The Nervous System.*—Asthenic patients are usually quick, impressionable, emotional, but lacking in self-control and break down under sustained effort.

Doubtless the comparative immunity of children may be explained by the activity of child life. In especially well-cared-for, well-nourished individuals of both sexes, leading well-ordered lives, no nervous manifestations need appear. As a whole, asthenic individuals are peculiarly vulnerable to tuberculosis, and at all ages bear acute diseases less well than normal individuals. With them the putting on of flesh means improvement, and so long as they retain this they remain well. Undoubtedly asthenic children are born of asthenic parents, but proper feeding, bathing, clothing and exercise are the chief requisites.

The treatment of active symptoms resolves itself into two chief factors: (1) the improvement of nutrition; (2) the proper use of suggestion. There is absolutely no limit to the pain manifestations of asthenia, yet, whatever the location and however great the intensity, they disappear like magic under rest and proper nutrition. Suggestion is carried out along the usual lines for neurasthenic cases, and as soon as the patient has gained several pounds beyond her previous maximum, or at least been brought up to it, more active exercise is gradually begun and continued from day to day until the patient is taking a large amount of exercise, but holding and even gaining weight. The writer firmly believes that this treatment should be adopted in the care of all patients who are able to pay the necessary hospital charges and special nursing fees. In other cases a change from the city to the country, or even rest at home with increased feeding, may prove sufficient, but in the writer's experience such cases seldom completely recover and are either failures or remain more or less invalided and subject to relapses.

## DISCUSSION.

*Dr. Fisher* said that these patients were most interesting from an emotional and educational standpoint. They can do much work and remain useful members of their families for life if they keep within a certain limit. If they overstep this limit they begin to lose weight and run down, not acutely, but slowly and progressively. The prognosis depends largely upon the willingness of the patient to carry out the details of treatment and upon the personal influence of the physician. In general, he was not inclined to take an unfavorable view of such cases. As to accomplishing a cure by the surgical correction of visceral ptoses, he had been impressed by the large proportion of cases in which operation failed to produce beneficial results, and he was rather against than for operation, unless there were very clear and distinct indications for surgical interference. This was particularly true of uterine operations. The visceral abnormalities were but rarely the cause of the asthenia, and surgery was therefore by no means a cure-all for this condition.

*Dr. Blackader* said these cases were not uncommon, but it was only recently that we had come to recognize their importance. He referred particularly to the cases occurring among children. The future welfare of such children depends almost entirely

upon what is done for them in early life. Many of them are overpressed at school, they get imperfect sleep, and they have poor teeth which are not properly attended to, in consequence of which they suffer from impaired digestion on account of imperfect mastication of the food. The future for them is dark, unless we can succeed in lightening their mental work and secure for them sufficient sleep and proper nutrition. Attention should also be given to a careful training of their emotional tendencies.

*Dr. Osborne* asked for information on one point. Almost every neurasthenic, especially if the patient is a woman, has some sort of abdominal disturbance. Now, if we made a diagnosis of loose kidney in one of these cases, should the kidney be fixed or not? We all knew that these patients improve after almost any kind of an operation, and he was not sure but that many of them would improve whether the kidney was returned to its normal position or not. He would like to hear from Dr. Morris on this point.

*Dr. Morris* said he had seen several of these patients operated upon when the operation should never have been performed, and he had said more than once that, if surgeons wished to avoid discredit in this line of abdominal work, they must differentiate the cases of congenital defect from recent, acquired, or traumatic cases. In reply to Dr. Osborne's question, he said that whether or not the kidney should be fixed depends upon the amount of harm that it is actually doing to the patient. If the loose kidney presses upon the pylorus or leads to torsion of its vessels or of the ureter, and thereby produces untoward symptoms, it should be fixed; but if it has no such range of motion and the pathological condition is discovered merely by accident in the course of an examination of the abdomen, there being no reason to believe that it is doing the patient any harm, there is no indication for surgical interference. In other words, if the loose kidney is actually doing the patient harm or is a menace to her safety, it should be fixed in its natural position; but the operation should not be performed just because the patient is discovered to have a loose kidney. He asked Dr. Greene whether he had noted the proportion of cases in which there are present other congenital stigmata, like high arch of the palate, imperfect development of the thyroid gland, etc.

*Dr. Wilson* said that surgeons had too often advised operation for the relief of the symptoms mentioned by Dr. Greene. They are now coming to realize that operations for the relief of symptoms in neurasthenic patients are not only productive of no real good in most cases, but often make the condition of the patient worse than before. The danger now is that the pendulum will swing too far in the opposite direction, and that some worthy cases will be denied needed surgical treatment. While scientific physicians realize that generalizations are sometimes necessary, they always keep clearly in mind the fact that the patient must be studied and treated as an individual.

*Dr. Satterthwaite* asked Dr. Greene to state his views concerning the relationship of intestinal affections, particularly mucous colitis, to these cases. He often found that if he devoted his chief attention to the intestinal tract, giving high enemata, etc., he succeeded in relieving not only the local symptoms, but also the general neurasthenic condition as well.

*Dr. Morris* inquired as to the significance of displacements of the colon.

*Dr. Gallant* said that in these cases the colon must go down before the stomach. Upon vaginal examination we could sometimes feel the colon in the *cul-de-sac*. He recalled particularly one instance of this kind. Under these circumstances the mucous colitis was readily explained. Nearly all of the patients suffered from these conditions in a chronic form. He is now treating a patient who has been in a sanitarium for four weeks with marked hallucinations. Her husband states that she has had them before also. Her bed is raised ten inches at the foot and she is being overfed, and he hoped by posture and medicinal treatment to get the stomach back into place. If he did not succeed in this he intended to operate and free the dilated stomach from its adhesions, and thereby replace it manually. He believed that something definite should be done, or this patient

would lose her mind. According to his experience, when the stomach was thus freed it promptly collapsed, and did not dilate again. The weight of the colon was largely responsible for the dilatation and ptosis of the stomach. He did not know how the adhesions had originated in the case referred to. All that the patient could mention by way of explanation was that she had had an attack of typhoid fever some time ago.

*Dr. Greene*, in closing, said that in treating these cases we should remember that we are dealing with a systemic lack of vitality affecting the whole body. This is the key to the symptomatic relationships. Christian Science sometimes does good in these cases, just as the physician does good by hopeful suggestion; but, on the other hand, it is liable to do irreparable harm by causing the patient to defer needed treatment. In answer to Dr. Morris's question, he said that thyroid stigmata are rarely present. Arched palate, however, is frequently observed. As to the effects of operation, he had formerly been over-generous to the surgeons in this class of cases, but in the last few years he had found it increasingly difficult to select the really operable cases. Of course, if the kidney caused ascites or other harmful symptoms by pressure or otherwise, it should be replaced, but for the most part he now found that operation was needed less and less often, since he had been treating the patients by rest, posture, etc. These patients are peculiar in the readiness with which they develop symptoms referable to the various organs. This can probably be accounted for in part by their lack of general vitality. Improve the vitality, and the symptoms disappear. The weight is the best guide as to the results of treatment. Nearly all the patients present symptoms of gastric neuroses and are under weight. In most cases the loss of weight has been gradual. With an increase in weight the symptoms improve; when it is stationary or falling they remain *in statu quo* or get worse.

# FURTHER USES OF SOLUTION OF CALCIUM CREOSOTE IN MEDICINE.

By LOUIS KOLIPINSKI, M.D.,

WASHINGTON, D. C.

THE communication ("The Therapeutics of Calcium Creosote") presented at the meeting of the American Therapeutic in 1909 tells of the preparation of this remedy and of its various properties; also of its successful use in croupous pneumonia, typhoid fever, cholelithiasis with septic fever, scrofula, the pretuberculous state, and summer diarrhœa of infants, and in the medical treatment of appendicitis and of several other ailments. The article concludes by saying: "This form of creosote possesses perhaps other virtues than those here described, and may be found to be very useful in other systemic affections and local pathological changes, not alone by its internal administration, but by topic application. Dermatology seems to be a field inviting a fair and varied trial."

Here now follows an account of further uses of solution of calcium creosote in medicine. The greater part of these practical observations were made in the past twelve months. Calcium creosote yields a non-toxic alkaline antiseptic solution, and is therefore superior to corrosive sublimate, phenol or boric acid as a menstruum in surgical work, for the preparation of instruments, and as a wash, liquid dressing, and irrigating fluid for wounds of operation or injury. Its effect on sensation is bland or more or less analgesic. Undiluted, it produces no appearance of irritation or inflammation of the integument, although applied for days. In practice it may be used of ordinary strength and specific gravity or diluted with one to three volumes of water. It may well supplant the antiseptics mentioned and others in routine surgical technique. It can also be applied with great advantage in acute and chronic inflammatory processes and in various ulcerative lesions of mucous membranes. In pharyngitis, and catarrhal, follicular or suppurative tonsillitis it can be used of normal strength or diluted as a gargle, or with a spray atomizer. It must be applied freely and repeated every hour or two. In the several forms of chronic nasal catarrh it may be exhibited daily. Here it markedly reduces morbid secretion and crust and scab formation. On account of its analgesic property it can be made the means of affording great relief in laryngeal tuberculosis and in cancer of the tonsil or fauces, while in painful inflammatory processes of the tongue, aphthous stomatitis, and oral syphilitic mucous patches it relieves and heals when used as a mouth wash. A chancroid frequently mopped with calcium creosote solution or immersed in it several times a day heals rapidly, and associated chancroidal bubo subsides at the same time without suppuration, provided the treatment is begun early enough.

*Syphilis.*—A chancre treated in the same manner likewise heals, but

more slowly, and the induration of the base of the ulcer remains. The reactions of these distinct infections under this treatment can be made of use in determining the nature of the sore and the necessity of future internal treatment. In syphilis, besides healing the primary lesion, it is beneficial in the sore throat and in necrotic gummatous ulcer of the skin. In neglected cases this lesion on the lower extremities is usually accompanied with the fœtor of gangrene and with acute pain when badly dressed. The use of calcium creosote locally gives very speedy relief by inaugurating the process of healing. It will be found in practice a grateful adjuvant to the proper systemic treatment of the disease.

In gonorrhœa of the male, given internally, it is without result. As an injection in the same disease it was not tried for the reason that all methods of injection treatment as yet employed can be held unsafe. In females with acute gonorrhœal endometritis extending to the Fallopian tubes and the ovaries, with fever and the tenderness and pain of acute pelvic peritoneal inflammation, given internally at two-hour intervals, it soon brings the temperature to normal, and with the fever is abolished all subjective discomfort. In gonorrhœal rheumatism in both sexes, when acute, its effects are similarly prompt and happy. As long as the joints are swollen and red much relief can be given by inunctions of precipitated sulphur with cocoa butter, one to eight, but the internal frequent giving of calcium creosote rapidly abolishes the fever and exquisite tenderness. The benefit afforded is obvious, as the case recovers rapidly, without recurrence and with no stiffness of joints or tenderness remaining.

In dermatological practice it will be found to have useful and varied properties. Chronic eczema of the hands results from such daily work as is a persistent irritant to the integument, *e.g.*, in bakers, plate printers, machinists and others. It is often found with consumptive ancestry, and the skin is then pale and thin, with scant or no subcutaneous fat. This chronic eczema is also found in adult consumptives, and is very probably a tuberculous lesion. It persists in an indolent and obstinate form for years.

*Calcium creosote as a wash,* one to one or two of water, or in full strength, by means of a wet compress, is here an excellent application, resulting in a cure. Varicose ulcer of the leg is rapidly made sterile and begins to heal under its use by a compress. In the smaller ulcer about the ankle-joint, which is the most painful form, the pain is quickly abolished by it. Cicatrization is completed by the employment of a dry desiccant powder and an appropriate bandage or elastic stocking. In excessive and offensive sweating of the feet, calcium creosote, used for fifteen minutes twice a day as a foot-bath, will control this otherwise inveterate and harassing morbid function. In eczema seborrhœicum, seborrhœa oleosa and seborrhœa sicca affecting the scalp, the hair becomes dry and has a tendency to fall out. In males there is a marked inclination to baldness, and in both sexes a profuse production of dandruff. In this common and inveterate form of skin disease calcium creosote solution, when rubbed undiluted into the scalp on retiring at night, is curative and prevents its reappearance. Under its action the hair resumes

its natural luster and ceases to fall out. Incipient baldness disappears, and the scales of dandruff, the patient's main annoyance, cease to form. While treatment of such maladies is possible with a variety of antiseptics, and sulphur is held by many to be highly efficient, the calcium creosote seems superior to all these for ease of application and surety of result.

In diabetic gangrene of the extremities and in diabetic ulcers boric acid in solution with sodium biborate is a good remedy, but calcium creosote, diluted one-half, is superior to it because it mitigates the severe neuralgic pain, causes desiccation of the dying and dead tissues, promotes a line of demarkation, and destroys the smell of putrefaction. The use of wet compresses with an impervious outer covering is the most practicable manner of applying the solution. If the patient is moribund it is an application of the greatest efficiency for the comfort of the sick-room, while, if surgical amputation is proper, it renders the wound aseptic.

In psoriasis it is used in the same way, a cover of oil-silk being applied when the patient retires at night and the compress rewetted once where practicable and removed on arising in the morning. The psoriasis of the scalp is treated in a similar manner or with washing, repeated if possible several times daily. The hair should be clipped or cut very short. As a result, the abundant desquamation and the itching cease. The psoriatic patches no longer expand and coalesce, and the affected area resumes its normal color, though a slightly thickened border is apt to remain for some time. The compresses must be continued until the most careful search of the skin can find no trace of the disease remaining. In this affection internal treatment is futile, and may even aggravate the condition.

In lupus vulgaris, when the process is broken down and suppurating, if calcium creosote is given internally, the discharge greatly diminishes and raw, ulcerated excavations appear. These are prone to bleed and are buried under a thick, hard incrustation which is repeatedly dropping off and re-forming, and they finally heal with great slowness, leaving deep-red, very shallow cicatrices, which ultimately turn white. When the lupus nodule is intact, a pearl-white particle in the skin, calcium creosote produces another reaction. The nodule grows red, then purple, swells up, becomes loose, and is thrown off as a necrotic patch, leaving an ulcerated cavity to heal, as just described. This succession of changes may require months, and is similar to the phases natural to the life history of a tubercular granuloma. Here, however, the one or the other series of changes starts within a few days after beginning the calcium creosote. Lupus with heavy crust formations is quite painful, and in hot weather the seropurulent secretion is much increased. These symptoms are rapidly diminished by this remedy. With the destruction of visible tubercular nodules the process of slow healing begins, but the expectation of a cure may be marred by the appearance of a fresh efflorescence of granulomata here and there at the periphery, causing a slow extension of the disease, with a repetition of the process described. It cannot, therefore, be said that calcium creosote cures lupus, but rather that it destroys the developed neoplasm. In most lupus patients the disease lasts for many years,

while, in some, visceral tuberculosis rapidly destroys life. Time and cases have been wanting to observe the ultimate results from treatment with calcium creosote. The remedy is given in full doses, four to six times a day, and is continued for months. The process of destruction and healing can be greatly expedited if at the same time compresses wet with it are kept steadily applied. The pain of the ulcerations, however, is apt to render this local treatment more or less interrupted and irregular.

*Other Conditions.*—In gastric ulcer it may be used, in aid of the milk diet treatment, as an antiseptic and as an antacid. In cancer of the œsophagus, stomach and pylorus, where surgery has failed, and in the hopeless stages of the disease, much relief can be afforded by means of a teaspoonful of the solution every two or three hours. It checks vomiting and obtunds the incessant pain; so that morphine is needed less where calcium creosote is used. It also moderates the frequency and volume of gastric hæmorrhage. At the end the patient expires from the exhaustion of inanition without the distressing suffering commonly observed in these cases. As a palliative in these incurable cases it is greatly superior to the ordinary narcotics. In the first paper it was stated that, in Pott's disease, hip-joint disease, and tuberculosis of the knee, the ankle and shoulder joints, great improvement has been repeatedly seen after its use. So markedly is this the case that in the treatment of these bone and joint lesions, splints, fixation and extension apparatus, and confinement to bed are employed in addition only in instances where there are urgent special indications, such as intense pain or paralytic loss of function. On the contrary, the patient is allowed to walk about when able, or even to follow his daily occupation. Calcium creosote diminishes pain, lessens caseation and suppuration, and improves the nutrition. It appears to oppose directly the development of the fatal amyloid degeneration. It is a clinical mystery, and a much greater disappointment, to observe how such a remedy, which presents such strikingly favorable results in this variety of a disease with a specific parent cause, in pulmonic and other visceral forms of the same is productive of no benefit, unless it be in that early precursory stage where no disease process has as yet begun, and only hereditary or other predisposition may make one assume that tuberculosis will develop.

Several correspondents have expressed the apprehension that calcium creosote solution may be an irritant to renal structure or function because of the large quantity of creosote the dose contains. This is a groundless fear, as no appearance of pathological change has ever been found in urines from many patients examined at short intervals with the special purpose of detecting any damage the kidney may have suffered. In typhoid fever and pulmonary tuberculosis where the solution is given daily to the amount of three fluidounces, and continued for weeks, the urine shows no variation from the conditions which are found in these diseases when it has not been administered. In subacute and chronic nephritis it does not increase the albumin, while in renal hæmorrhage it checks the bleeding. On account of its very pronounced antiseptic power, the gastrointestinal symptoms of uræmia, such

as flatulence, nausea, vomiting and malaise of indigestion, are relieved. While no good effects have been observed to occur from its use in the different forms of inflammation of the kidney and the sequences thereto, on the other hand, no injury to the integrity of the renal gland has been noticed.

From all of these observations it is evident that calcium creosote does not "fill a long-felt want" or is either a wonderful medicine or a cure-all. It is not heralded as a specific in any one of the many maladies in which it has been given with fair success. It is, however, plain that it can be used daily by the practitioner in a great variety of diseases with favorable effects and great satisfaction, and that it can very efficiently replace a number of other and similar drugs which possess, besides curative properties, harmful and toxic ones. Success in prescribing depends on judgment in selecting efficient drugs which are free from unpleasant side-effects and which also the patient declares to be helpful to him. From this standpoint the remedy here discussed will not lack friends and advocates.

## DISCUSSION.

*Dr. Barton* inquired as to the chemistry of calcium creosote. Was it a mixture or a true compound of creosote? Was it the calcium or the creosote element which produced the beneficial results? As to the effects of creosote in tuberculosis, this opened up a question which seemed to have been long closed. The weight of evidence tends to show that creosote is of little value in pulmonary and other forms of tuberculosis so far as its effects upon the tubercle bacilli themselves are concerned. Any benefit which may result from its use is probably due, in a large measure, to its effect upon the intestinal contents, as in the case of any other intestinal antiseptic, and the pulmonary effects are secondary.

*Dr. Morris* related an anecdote about his old preceptor who came in hurriedly one day and told him to visit a patient for him. Dr. Morris asked what he should give her, and his preceptor replied, "Anything, so long as you give it to her with confidence." He said he also would like to know more about the chemistry of this substance, and inquired particularly as to its effect upon leucocytosis.

*Dr. Kolipinski*, in closing, said he was unable to explain just how the remedy produced its beneficial effects in tuberculosis of the joints and skin. He did not advocate its use in pulmonary tuberculosis. As to the chemistry of calcium creosote, he had described its physical and chemical peculiarities in a paper read before this Society last May. It is not a strong chemical compound, but appears to be a basic calcium salt. It is decomposed by air and light, and in some particulars acts like calcium hydrate. It affords a convenient and effective method of administering creosote. Creosote, alone, is irritating to the stomach, but, when combined in this way, it loses its irritating properties to a very great extent.

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# SKIN INUNCTION AS A THERAPEUTIC MEASURE.

By LAWRENCE F. FLICK, M.D.,
PHILADELPHIA.

INUNCTION as a health measure goes back very far in the history of mankind. The Romans practised it in the heyday of their civilization and we have reason to believe that they borrowed the practice from older nations. In the greasing of the skin by some of the wild tribes of the present day in various parts of the world we have the suggestion that at a very early time it may have been a general practice by all peoples. Inunction for the purpose of medication was apparently also practised in very early times by the Eastern people at the height of their civilization. For just what conditions they used it we do not know.

Theoretically, inunction ought to be one of our best therapeutic measures in chronic diseases, because it enables us to apply the medicine which we wish to give in a slow, even, continuous manner through the largest organ of the body. To get medicine into the system in this way is particularly valuable in diseases in which recovery depends upon a long, tedious struggle of the cells of the body against an invading micro-organism. In such diseases medication which carries the remedies into the system quickly and in large quantities may do harm. This harm may not be direct, but may be indirect by interference with the physiological functions of important organs of the body. A drug, for example, which may even be tolerated by the tissues in large quantities may nevertheless interfere with digestion, assimilation and metabolism in such a way as to bring dire consequences upon the organism.

The skin is a very important organ in the economy of the body. It has many functions, some of which are very closely concerned with metabolism and nutrition. It excretes waste products, it helps to maintain a normal temperature, and it contributes something to the equilibrium of the circulation. It has the power of absorption, not as one of its chief functions, but secondarily and for protective purposes. It exercises this power through the lymphatic system, which permeates every part of it. The skin all over the body is well supplied with lymph stomata and lymph channels which run toward central trunks and empty into the blood-stream. The lymph nodes under the skin and draining the skin are somewhat restricted in their distribution and are found principally in the groin and the axilla. Absorption can undoubtedly take place in every part of the skin, although it is probable that it takes place more rapidly in those parts in which the lymph nodes draining the skin are situated. Inunction may therefore be made in every part of the body, but should be practised particularly in the axilla and the inside of the thighs.

The disease in which medication by skin inunction has received most general recognition is syphilis. Mercurial inunction in syphilis has been a well-recognized practice for a good many years. The system can be brought

under the influence of mercury quickly in this way, and the influence can be maintained more evenly than by any other method of medication. The practical results have been excellent, perhaps the best obtainable.

For twenty years I have used the inunction method in the treatment of tuberculosis, having taken up the method on theoretical grounds, and my experience with it has been most satisfactory. I have applied iodine in this way. From time immemorial iodine in some form or other has been recognized as a valuable remedy in tuberculosis, but there has always been some difficulty experienced in its use on account of its disposition to upset the digestive tract and in that way interfere with nutrition. When I began to use iodine by inunction iodoform had some reputation as a remedy in the treatment of tuberculosis, and in using that drug I had gotten the impression that it frequently disturbed digestion and assimilation. I hit upon the idea of inunction and found it quite easy to dissolve iodoform in codliver-oil and olive-oil and get it into the system by rubbing this solution into the skin. The results seemed better than any that I had obtained with the drug by the mouth, and really seemed better than any that I had obtained by any other medication given in any way whatsoever. Incipient cases of tuberculosis seemed to recover under these inunctions in a relatively short time; so short, indeed, that one got the impression that recovery depended upon the inunctions. There was one serious objection to the treatment, namely, the odor of the iodoform, and this objection could not be overcome by any disguise that could be given to the drug. So good were the results, however, that people who had used the inunction were in practically every instance willing and glad to continue it in spite of the odor, which attracted attention everywhere. A few years later when cresol iodide was put into the market I found in it a satisfactory substitute for iodoform in effectiveness of treatment, with the advantage of freedom from odor. I have since then used cresol iodide inunction as a routine treatment in all cases of tuberculosis. Like iodoform this substance gives striking results. I have never been able to demonstrate that these results are due to the iodine, but everyone must recognize the difficulty of doing this in a disease like tuberculosis, in which there can be no standard of pathological conditions and severity of the disease and in which nature itself does so much for recovery that it is impossible in any given case to differentiate between what nature has done and what may have been accomplished by medication. All that one can do in this disease is to give an honest opinion as to the value of any drug or method of treatment, and let that stand for what it is worth. After a long experience with iodine inunction in tuberculosis I am convinced that it is a valuable method of treatment.

There are other forms of iodine besides cresol iodide and iodoform which can be used for inunction. Iodized oil, which is much cheaper than solution of cresol iodide, gives satisfaction, although it does not seem to me to be as useful as the latter. I have an idea that part of the value of cresol iodide and iodoform lies in breaking down after absorption, with production of nascent iodine, but for this view I have nothing but an impression. There are quite a number of iodine compounds similar to these two which may

be used, but some of them break down too rapidly and others too slowly. The preparation should hold up long enough in the oil to enable the patient to have a fair quantity put up at one time, without having it spoil for him. There are preparations which are much richer in iodine than cresol iodide, and which would probably be more valuable for inunction purposes were it not that they break down almost immediately when dissolved in oil, and therefore give practically an iodized oil. Most iodine compounds are soluble in codliver-oil and olive-oil in the proportion of about one dram to two and one-half ounces. In essential oils, such as oil of anise, oil of gaultheria, and the like, they are soluble in the proportion of one dram to two ounces. They have about the same solubility in hydrous wool-fat. In prescribing preparations of this kind an effort should be made as far as possible to make them agreeable and pleasant to the sense of smell. Some of the formulas which I have used with satisfaction are as follows:—

℞ Cresol iodid. ..... ʒij.
Ol. rosæ ..... gtt. ij.
Ol. anisi,
Ol. gaultheriæ, of each ..... fʒij.
Ol. olivæ ..... q. s. ad fʒv.
M. Sig.: Rub into body as directed.

℞ Cresol iodid. ..... ʒij.
Ol. anisi,
Ol. gaultheriæ, of each ..... fʒij.
M. Sig.: Rub into body as directed.

℞ Cresol iodid. ..... ʒij.
Ol. gaultheriæ ..... fʒij.
Adip. lan. hydros. ..... ʒiij.
M. Sig.: Rub into body as directed.

A secondary effect of the inunction which perhaps contributes a good deal to its usefulness is the stimulation of the vasomotors in the skin by the rubbing and the gaultheria. With a view of increasing or diminishing this influence the amount of gaultheria can be increased or diminished. It is quite possible, too, that the gaultheria itself may have a medicinal influence, as may also the oil of anise. The gaultheria is particularly valuable in those cases in which patients complain of a great deal of pain, more or less fugitive in character, in various parts of the body, probably due to the absorption of toxins from some of the micro-organisms which produce mixed infection of a kind which is non-febrile.

In recent years I have extended my inunction treatment with marked benefit to the pharynx in those cases in which there is a chronic granular pharyngitis. In tuberculosis this unhealthy condition of the lymphatic tissue of the pharynx and the post-nasal pharynx, apparently due to a mixed infection of some character, occurs quite often. It is a great source of annoyance to the patient, and appears to be an impediment to recovery. It is a troublesome condition which does not readily yield to treatment. I have found inunction of these parts, especially around the tonsils, with a saturated solution of cresol iodide in equal parts of oil of anise and oil of gaultheria the most effective treatment with which I have had experience. I apply the oil on a pledget of cotton, rubbing it in with considerable vigor.

# REMARKS ON HEXAMETHYLENAMINE, WITH ESPECIAL REFERENCE TO THE ELIMINATION OF THIS SUBSTANCE IN THE SECRETIONS FROM THE MIDDLE EAR AND NASAL SINUSES.

## Application to the Treatment of Diseases of these Organs, with Illustrative Cases.

By WILFRED M. BARTON, M.D.,
Professor of Pharmacology and Therapeutics in the Medical Department of Georgetown University,
WASHINGTON, D. C.

In an oral communication Dr. Barton gave an account of some recent work on this subject. He had made a preliminary report on the subject in an article which had been published in the *Journal of the American Medical Association,* March 12, 1910.

The first part of the report dealt with generalities concerning the drug hexamethylenamine.

*Historical.*—Hexamethylenamine was first made by Butlerow, in 1860. Nicolaier, in Germany and Bardet, in France, simultaneously worked out certain clinical aspects of the drug. The names of Casper, Elliott, Loebish, Orlowsky, Kelly and Wilcox are intimately associated with its earliest use, at the time which might be called the era of genitourinary application of the drug. It was first recommended by Nicolaier to prevent deposit of urates. Casper soon extended its use to ammoniacal fermentation of urine, and, as a result of the combined researches of Nicolaier, Casper and others, it was widely employed in cystitis, pyelitis and infections generally of the urinary tract. In a few years its use was extended to the treatment of bacteriuria in typhoid fever, to prevent cystitis and insure against propagation of the disease by the urine. Soon afterward it was employed as a prophylactic of scarlatinal nephritis and as a prophylactic in operations upon the urinary tract (Casper). The era of extension of the use of hexamethylenamine beyond diseases of the genitourinary tract began in 1908 when Crowe, of Johns Hopkins University, showed that the drug is eliminated in the bile and pancreatic secretion and demonstrated experimentally and clinically its applicability to the treatment of infections of those tracts. This important discovery of Crowe was followed the next year by one equally important by the same investigator, that the drug is eliminated in the cerebrospinal fluid and that it is of great use particularly as a prophylactic against infections of the meningeal tract.

*Chemistry.*—Hexamethylenamine is a condensation product obtained by passing dry ammonia gas into formaldehyde. Reaction takes place thus: $6CH_2O + 4NH_3 = (CH_2)_6N_4 + 6H_2O$. On heating the drug with $H_2SO_4$ and $Fe_2Cl_6$ formaldehyde is liberated. The substance is very soluble in water, and its solution gives an orange-yellow precipitate with bromine. The reaction

for the detection of hexamethylenamine depends upon the liberation of formaldehyde from it by means of $H_2SO_4$. A drop of milk is added to the suspected liquid, to supply casein, and the reagent (100 c.c. $H_2SO_4$, 96 per cent. + 2 gtt. 3 per cent. sol. $Fe_2Cl_6$) is poured into the tube. At the line of juncture an amethyst color appears (Crowe).

*Physiological Action.*—The drug may be detected in the urine in ten or fifteen minutes after its internal administration. Half a gramme will be eliminated in about half a day. Animals are very tolerant. Ten grammes in a rabbit produced albuminuria, and 15 grammes in a dog produced hæmaturia. Fleig (1907) showed by onconometric observations on the kidney that primary vasoconstriction, followed by vasodilation, is brought about in the kidney.

*Bacteriological Power.*—Orlowsky, of St. Petersburg, found that hexamethylenamine inhibits the growth of cholera vibrio, staphylococcus and Siberian pest bacillus, but that its action in this respect is less than that of mercuric chloride or phenol. Also that albuminous substances interfere with the development of the antisepsis, and, finally, that fermentative organisms of urine are killed at body temperature. Nicolaier found that it acted on culture media only at body temperature, and concluded that the antiseptic effects are due to liberation of formaldehyde. This opinion has been opposed (Götzl), and the question is not yet settled, though the opponents of Nicolaier's theory appear to have the best of the argument.

*Toxicology.*—The drug is not poisonous, but in man some undesirable effects are known to have occurred. Beardsley's article in the *Therapeutic Gazette* is quite complete on this subject. Hæmaturia is the most common complication, and the occurrence of this symptom does not appear to always coincide with the size of the dose. Albuminuria is a rare symptom, and the same is true of skin eruptions. Gastrointestinal disturbance (pain, diarrhœa) has also been noted.

The second portion of Dr. Barton's communication related to his own investigations upon the treatment of suppurative otitis media and sinusitis by hexamethylenamine. He had had 7 cases under his observation. The first was the one in which he had first demonstrated that the drug appears in the discharges from the middle ear. Dr. Mead Moore, of the Episcopal Hospital, Washington, D. C., soon afterward obtained a positive reaction from a patient with suppurating sinusitis to whom the drug was administered. The details of the observations were not given by Dr. Barton, since they were to appear in a separate communication. The summary of conclusions deduced from his experiences was as follows:—

1. Hexamethylenamine is eliminated by the mucous membrane of the middle ear and accessory nasal sinuses.

2. The drug is of service in acute suppurating otitis media, all the cases being apparently rapidly cured. The chronic cases were ameliorated, no absolute cure having been noted in a limited number of cases.

3. Upon *a priori* grounds it may be assumed that hexamethylenamine may prove to be a valuable prophylactic in those diseases commonly attended

by otitis media; perhaps also as a prophylactic used prior to surgical operation upon the middle ear or mastoid and the sinuses of the nose.

## DISCUSSION.

*Dr. S. L. Dawes*, Albany, N. Y., said it seemed to him that no drug which had been introduced in the last decade gave greater hopes for the future than hexamethylenamine. If we have found a drug which will serve as an effective antiseptic in otitis media, a great advance has been made. Hexamethylenamine possesses the valuable property of acting as an antiseptic during its elimination from the body. After its administration we find it in the cerebrospinal fluid, bile and urine, and in the secretions of the middle ear. The fact that it does much good through its elimination by the kidneys in phosphaturia and certain bladder affections is generally recognized. The exact manner in which it produces its beneficial effects is not known in all cases, but it must have some definite bactericidal power, and this suggests that it may prove of service in many diseases in which it has not yet been tried.

*Dr. James A. Gannon*, Washington, D. C., said he was among the first to whom Dr. Barton described his valuable discovery with regard to the usefulness of hexamethylenamine in middle-ear troubles, and at Dr. Barton's suggestion he decided to give it a trial in his clinic on Diseases of Children at Georgetown Hospital. He had employed the drug in some 15 or 20 cases, and had had no disappointments. He briefly described the results obtained from its use, and referred particularly to a case of chronic otitis media of one year's duration in a child 3½ years old. This patient had been treated in the usual way with irrigations, tonics and hygienic management, but had failed to improve. She was under weight, had a fetid discharge from the right ear, and tenderness around the ear. Boric acid irrigations, t. i. d., and hexamethylenamine, 1½ grains, four times a day, were ordered. In two days the odor of the discharge had disappeared, and in four days the discharge ceased entirely; so that the irrigations were discontinued, while the hexamethylenamine was gradually reduced and finally discontinued. This child has had no discharge for a month, and has improved rapidly in health. Dr. Gannon had used hexamethylenamine in earache, especially during influenza, with prompt disappearance of the pain. He considered the drug not only an excellent curative agent, but a good prophylactic.

*Dr. Osborne* said that Dr. Barton's experience tended still further to substantiate the conclusion which had already been pretty generally reached, namely, that hexamethylenamine is a valuable addition to our materia medica. How long can it be used without danger of harmful effects? He has had a patient with locomotor ataxia under treatment for a year and a half. He had suffered from phosphaturia for from six to twelve months before he came under observation. Dr. Osborne tried every measure he could think of to relieve this condition, but without success until he used hexamethylenamine, and from that time the phosphaturia has given no trouble. Although the patient has now been taking the remedy for a year and a half, thus far no unfavorable effects have been noted. At first he gave him 0.50 Gm. four times a day, and then gradually reduced the administration to once a day. This did not hold the phosphaturia in check, however, and he was obliged again to give the remedy oftener.

*Dr. Fisher* reported a similar case in which he had used the drug for four years. He had seen no bad effects from its prolonged use.

*Dr. Stewart* asked what would happen if formaldehyde should be set free in the blood as a result of the decomposition of the hexamethylenamine.

*Dr. Barnes* said that Dr. Barton's discovery had already proved of great service in hospital and dispensary work. Clinically the effects of the drug were all that could be desired. He reported a case of chronic suppuration of the middle ear of two years' standing. As a result of the administration of this remedy the secretion first became more fluid, and then lost its odor, and yesterday there was no sign whatever of a dis-

charge. He had given hexamethylenamine with beneficial results to all of a family of four children with chronic ear disease, one of whom had been treated surgically. Even in this last case, although the temperature ran high, no pus appeared, its formation having apparently been prevented by the remedy. It is remarkable how the drug controls the discharge in these cases. Its beneficial effects open up a field of usefulness in the ear complications of grippe, scarlet fever, measles and other diseases. In these infectious diseases hexamethylenamine should be given for its double prophylactic action, the prevention of kidney, as well as middle ear, complications.

*Dr. Leech* spoke of the great value of hexamethylenamine in the prevention of the kidney complications of scarlet fever and other infectious diseases. He employed it regularly in most of his cases, and he had also used it successfully in gonorrhœa and during pregnancy.

*Dr. Morris* said that we hesitate to use the bacillus vulgaricus in certain forms of suppuration for fear that it may become the dominant species. If, however, we could control its growth by the use of hexamethylenamine, we should open up a valuable field of usefulness of both of these agents. The drug acts favorably in scarlet fever by inhibiting the colon bacillus nephritis, thus ending kidney complications. It would be interesting to know whether in the same way it destroys the bacteria which cause nephritis in some other diseases.

*Dr. Barton* said that, as to the fate of any formaldehyde which might be liberated in the blood through the decomposition of the remedy, he believed it would enter into combination with the proteid molecule, for which it has a marked affinity. He had succeeded in proving that formaldehyde is sometimes present in the aural discharge of patients suffering from chronic suppuration of the middle ear who have been taking hexamethylenamine.

*Dr. Morris* said that it was not so important to know how the drug destroys bacteria as it is to be sure that it actually kills them.

# THE RANGE OF ACTIVITY AND THE UNTOWARD EFFECTS OF CERTAIN SPINAL ANALGESICS; BASED ON TWO THOUSAND ADMINISTRATIONS.

By W. WAYNE BABCOCK, A.M., M.D.,
Professor of Surgery and Clinical Surgery in Temple University,
PHILADELPHIA.

In the two thousand cases were included all kinds of operations in all parts of the body. This kind of anæsthesia should properly be called nerve-root anæsthesia, rather than spinal, as it was the nerve-roots which were affected. Its safety depended largely on the height in the spine of the nerve-roots which it was necessary to narcotize for any given operation. The higher up they were, the greater the danger. The delicate thing was to have the solution employed sufficiently light to affect the sensory nerves without involving the motor ones. It could be made lighter by the addition of 10 per cent. of alcohol to 4 per cent. of solution. By regulating the position of the patient's body it was possible to arrest the anæsthetic at any point of the spine desired. The speaker considered the doses used by Jonnesco unnecessarily large, and said that the same results could be obtained from half the doses he employed. In all operations in the upper part of the body it was essential to be prepared to perform artificial respiration at any moment. In the cases embraced in the report various anæsthetic agents were employed.

## DISCUSSION.

*Dr. Osborne* asked what solutions he had found the most satisfactory for spinal anæsthesia.

*Dr. Barnes* inquired whether it would not be possible to inject at some point of the spinal canal a solution having the same specific gravity as the cerebrospinal fluid, so as to produce anæsthesia at a definite point; for example, in the region of the appendix.

*Dr. Morris* inquired whether the injected fluid would not eventually pass along the whole length of the spinal canal, in accordance with the law of the diffusion of liquids, whatever might be the specific gravity of the anæsthetizing solution. He had recently had a case, an osteoma of the frontal bone, in which spinal anæsthesia was used, and he found it necessary to keep the patient alive by artificial respiration for nearly an hour. During this time the outcome was a matter of great anxiety to him, but the patient finally recovered.

*Dr. Barton* asked whether the injection of a 10-per-cent. solution of alcohol might not have the effect of producing nerve degeneration, as alcohol was known to be a protoplasmic poison.

*Dr. Babcock*, in reply, explained that the alcohol content of the solution is reduced about one-half in strength through admixture with cerebrospinal fluid (withdrawn by the injecting syringe) before it is thrown into the spinal canal. No nerve degeneration has as yet been noted, although it has been carefully looked for. Such degeneration as has been noted within the last five years has invariably occurred in patients who have

been previously etherized. He cited a case of this kind, a child upon whom he had operated for tuberculosis of the knee-joint. Several weeks afterward meningitis developed. Nerve degeneration, particularly abducens palsy, occasionally followed the use of almost all of the synthetic alkaloids. Why the sixth nerve should be affected oftener than others he did not know. It pursued a longer course within the skull than any other nerve, and it was possible that this might have something to do with the explanation. The rate of diffusion of the injected fluid is very slow. The drug is decomposed by the cerebrospinal fluid, which still further limits its field of activity. The less alcohol used, the more rapid is this decomposition; hence as the fluid diffuses it decomposes, and the anæsthetic effect can be limited very largely to any desired portion of the spinal canal. Out of the 2000 cases in which he had used spinal anæsthesia he had met with only from six to ten where he had found it necessary to employ artificial respiration. One was an opération for the removal of the lower jaw. The dose recommended by Jonnesco had been given. Suddenly the patient stopped breathing, became pulseless, and was apparently dead. At the end of twenty-five minutes, however, during which time artificial respiration was administered, he gasped, and then soon recovered completely. Another was a case of shock. The patient was pulseless when he was put on the table, but Dr. Babcock was not informed of this fact by his assistant. He proceeded to give the intraspinal injection, and soon found it necessary to begin artificial respiration in order to keep the patient breathing. After ten minutes he went on with the operation, but the patient's respiration again ceased, and he had to give artificial respiration for six hours, at the end of which time the patient died. It seemed to him, however, that death was not due in this case primarily to spinal anæsthesia, for the reason that the effect of the injections lasts at most only two hours. Subsequently, though, he had a similar case, and since then he has had a third. He did not believe, however, that the final result in any of these cases was due to the anæsthetic. In reply to Dr. Barnes's question, he explained that at the present time spinal anæsthesia cannot be successfully employed for the purpose of anæsthetizing a certain small portion of the body. The cerebrospinal fluid itself varies in specific gravity, and it is impossible to estimate this in advance or to so place the injected fluid that only a small area, as, for instance, the region of the appendix, is made anæsthetic. In conclusion, Dr. Babcock discussed the relative value of the agents which are ordinarily employed at the present time for the production of intraspinal anæsthesia.

On motion of *Dr. Osborne* a vote of thanks was tendered Dr. Babcock.

# SENILE EPILEPSY.

By EDWARD D. FISHER, M.D.,
Professor of Mental and Nervous Diseases, the University and Bellevue Hospital Medical College,
NEW YORK.

UNDER this head I include only those cases which occur in adult life, and especially in the period when physical decline has already begun to show itself. The term epilepsy hardly applies here, but it is a name in use and cannot be discarded. The marked feature is the epileptic convulsion, as in essential epilepsy. The underlying cause is, however, essentially different, and marks itself out also by being usually localized in character, with, at times, a residual paralysis, which may last a few days, or an aphasia of short duration, if the seizure affects the right side of the body.

The underlying etiological factor is arteriosclerosis, which distinguishes it (absolutely) from essential epilepsy. The majority of cases coming under my observation have been men who have been very active in business life, perhaps inclined to good living, but not in any sense alcoholics, usually representing rather excessive brainworkers, characterized by their ability to manage large interests and little given to exercise or relaxation. Such men may be unusually vigorous and not aware of any excessive work or need of rest, reaching the age of fifty-five or sixty years without realizing that they have passed their youth and that the process of repair is not as rapid as in earlier life. There may have been few, if any, preliminary symptoms outside of some fatigue formerly unusual to them, or a slight weakness of memory for details or names, until, as out of a clear sky, an epileptic attack takes place, often without warning, perhaps following an exhausting day or a heavy dinner. Many of these cases are well nourished, although they may show signs of looking too old for their years. They may be addicted to stimulants in excess in the form of tobacco and coffee, and are often rather excessive meateaters. While arteriosclerosis is present, as shown in the external arteries, temporal and radial, and in the fundus of the eye, there is little evidence of kidney involvement, albumin and casts usually being absent.

We have then a type of man peculiar to our present modern life, of more than usual mentality, constantly engrossed in his business, with little variation and not given to social relaxation. As I have said, his life has been so preoccupied in prescribed lines that he scarcely knows that he has passed life's meridian and makes no allowance for the exhaustion of overwork on a system which no longer responds by rest to produce complete recuperation. The arterial tension is usually somewhat low unless there is stress of mental work, or excitement, or following ingestion of food. Just preceding the attack, however, the arterial tension is very high and is (without doubt) its exciting cause, or at least the preliminary condition just before the seizure. This

was especially marked in one case observed just before an attack. I have not included in this class of cases either those of alcoholic or syphilitic origin.

The course of the disease varies somewhat with the habit of life followed by the patient after his first seizure. The second attack may not take place for weeks or months. The exciting cause, then, may be given as due to exhaustion from overwork or some special excitement affecting the emotions, anger, or grief, but this is only the exciting cause; the fundamental cause is the arterial degeneration. Again, the seizures may be more frequent from the beginning, or there may be several seizures in succession, followed by a long interval before the next seizure. Other symptoms in the mean time are not marked, mostly being those of impaired memory for names and the more recent daily affairs of business. There may be some feeling of compression in the head, a dull, heavy headache rather than pain, and some dizziness. The arteries involved are probably cortical, the attack being due to temporary occlusion or stasis of the vessels, arterial or perhaps venous. There may be localized œdema or serous effusion, which, however, clears up, leaving no trace of paralysis or other impairment. There is probably a general arteriosclerosis of the cerebral vessels. The general tendency of the disease is toward dementia or premature senility, frequently accompanied by depression. The seizures may at times be very severe and suggestive of apoplectic attacks, and, in fact, may lead to or end in cerebral hæmorrhage of the usual type. I have no cases to report in which I have obtained an autopsy. The cases I report have been in private practice.

The differential diagnosis has to be made, especially in the younger cases, from general paresis or cerebral syphilis. The long course of the disease in many cases will aid us here, and the absence of pupillary changes found in specific disease is decisive; again, the negative Wassermann reaction is of diagnostic value. It is peculiar how few conditions present are indicative of organic changes in the arterial or venous systems, and yet how marked the clinical symptoms are in their progression toward mental deterioration. I shall detail 4 cases which may be of interest.

Case I. Male, sixty-three years of age, merchant, of temperate habits, with no specific history and very active in business affairs. He had not complained of illness. During rather an exciting period of business stress he was suddenly taken with a severe epileptic seizure involving the right side. He was supposed to have had a stroke. He made a complete recovery from this attack, with no evidence of paralysis remaining. He took a vacation and seemed well. Six months later he had a second seizure. The patient was very careful as to his diet. The attacks were never frequent, the patient going six months with but one seizure. During the last two years of his life he lived carefully, continuing in business and refusing all medication. The last seizure was apoplectiform, with convulsions, right hemiplegia, and death.

Case II. Male, fifty-five years old. His first attack was preceded by some mental disturbance. While on a business trip he became confused, lost the memory of his residence, became lost in his own city for a time and had a seizure with slight hemiplegia and aphasia lasting a few weeks. He made

a good recovery and returned to business, remaining apparently well for a year. He then had a second attack similar to the first. None of his attacks have been severe, but the patient has been excitable, irritable, egotistical and mentally incapable of doing business. A diagnosis had been made of general paresis, but the case has not progressed on these lines, there being no Argyll-Robertson pupil, though gradual mental weakness.

CASE. III. Male, sixty-five years old, merchant, no specific history. His first attack occurred in the morning and was very severe. Six months later the attacks became frequent, occurring every month. He gradually lost his memory, being unable even to remember his physician. He can, however, carry on routine business, but is gradually passing into dementia.

CASE IV. Male, sixty-eight years old, merchant. He had his first attack while in business. Each attack was due to some especial form of excitement. The patient was a heavy eater, but a very moderate user of alcohol and tobacco. His attacks lasted about half an hour, and he complained thereafter for several hours. He had little mental impairment, but still he was not the same man as formerly. His condition has improved with outdoor life and strict attention to diet and exercise.

The complete recovery from these attacks, although there may have been paralysis and aphasia present, shows that the cerebral condition is a temporary one. It is probably explained by the occurrence of a contraction of the caliber of the arteries, such as may be observed in the extremities, with temporary paralysis; the parts being ischæmic and œdematous. This has been observed in a case reported by Pal, in which the eye-grounds showed the arteries contracted and the veins empty; a condition which entirely cleared up after the seizure. It is an arterial condition similar to that which Russell described in an article entitled "Intermittent Closing of Cerebral Arteries; Its Relation to Temporary and Permanent Paralyses."[1] In temporary closing of the arteries there is impairment of function, a halting of brain function from the closing of channels which convey the blood, a condition comparable to intermittent claudication. It is a similar arterial condition to that which we find in angina pectoris, a spasm of the muscular coat of the arteries; or, again, as we find it in the splanchnic system, with a sudden seizure of great lumbar pain or colic, similar to the cardiac pain of angina pectoris.[2] In one patient under my observation these conditions seemed to be confirmed. The onset of the attack seemed to be great pain in the lumbar region, extending forward to about the umbilicus and into the extremities, with a complete paralysis of the legs. The pain was so extreme as to require morphine; at the same time there was a right-sided convulsion, hemiplegia and aphasia, with partial coma. All these conditions cleared up more or less completely, to be followed in a few weeks by an attack of angina pectoris. These seizures were caused, in my opinion, by arterial spasm and contraction. The patient was about seventy years of age, very active in business, and not addicted to any excesses. He

[1] British Medical Journal, October 16, 1907.

[2] Barker: American Journal of the Medical Sciences, May 29, 1910.

had arteriosclerosis with very slight interstitial nephritis and low arterial tension unless mentally excited or fatigued from close application to business.

The prognosis is not altogether unfavorable in a person not too far advanced in years and who is willing to let up in his work, take recreation in the open air, and change his mental activities somewhat.

The treatment consists in attention to the diet, lessening but not dropping the proteids, decreasing the arterial tension by the nitrites (and nitroglycerin), and giving sodium iodide in small doses continuously. It is not wise to remove these persons from business entirely; they should continue in active life in moderation. They should be especially warned against emotional excitement, anger, passion, or sympathy. Mental deterioration is often very rapid when, as is sometimes necessary, such cases drop all mental work. In anginal and abdominal attacks morphine is indicated, but only as long as relief is required; for a few days at most. Amyl nitrite often acts favorably. The bromides, if used, should be employed in small doses, 15 to 20 grains three times a day. The heart, again, may be the seat of myocardial changes, and strychnine and digitalis may be required, but should be used with caution.

## DISCUSSION.

*Dr. Williams* said that he had recently seen a case very similar to one of those described by Dr. Fisher. The patient was a man, 70 years of age, employed in one of the Government departments. The first attack came when he was in Utah at a high altitude, about a year ago, and he had had four or five since. He was a moderate eater of nitrogenous food and a careful liver, not given to the abuse of alcohol, and the nature of his business caused him to spend much of his time in the open air. The blood-pressure was only about 150 at the time of the attacks. There was no considerable degree of arteriosclerosis, so far as could be ascertained, except perhaps of the temporals. He advised the man to restrict his diet, especially as to nitrogenous food, cut down the purins, etc., and, as a result, he was now in very good health and had had no attack recently. From this it seems reasonable to conclude that even a moderate eater can sometimes be benefited by cutting down the diet, although of course the dieting should not be carried too far. It should be remembered that the aged require only a small intake of nitrogenous food. The body at this time of life is not in any condition to handle large quantities of proteid material. He also gave this patient iodides. He did not advocate the use of the nitrites in these cases; thinking it a better plan to attack the imperfect metabolism, the basic cause of the trouble. Recently Parker, as against Russell, has severely criticised the view that intermittent claudication, or spasm of the smaller arteries, is the cause of these attacks. He believed that sclerotic changes play an important part in their production, and that the mechanism is rather an œdema than a spasmodic anæmia.

*Dr. Osborne* said that he could not agree with Dr. Williams as to the effects of the nitrites in these cases. Those who treat many cases of heart and circulatory disturbance cannot endorse the laboratory results, which goes to show that the reduction of blood-pressure caused by the nitrites is but temporary. As a result of clinical experience he was convinced that a lasting depression of arterial pressure can be brought about by the frequent administration of the nitrites, even to a point where the use of a vasoconstrictor may be required. In treating these cases the physician should endeavor to keep the arterial pressure at the point where the patient is the most comfortable. According to his experience, sodium iodide gives the best results in 0.05 or 0.10 Gm. doses three or four times a day. In his experience the absolute withholding of meat in

the case of patients over 50 years of age, who had been accustomed to a full meat diet, was generally inadvisable.

*Dr. Fisher* said that the exact manner in which the attacks are brought about is, of course, a mooted question. The temporary duration of some of them, however, and the fact that the patients often recover without any permanent effects, cannot be explained by any permanent change of caliber of the cerebral vessels, such as would be likely to result from thrombosis. The character of the attacks would seem to demand an explanation involving a temporary cause.

# A CASE OF RECURRENT ABSCESS FORMATION, DUE TO STREPTOCOCCUS INFECTION, SUCCESSFULLY TREATED BY AUTOGENOUS VACCINES.

By GEORGE G. ROSS, M.D.,
PHILADELPHIA.

THE case herewith reported offers some interesting points in diagnosis and treatment, and will serve as a text for some remarks on vaccine therapy. It is one of staphylococcus bacteræmia with furunculosis, subperiosteal abscess of the scalp, and necrosis of bones of the skull, treated by operation and autogenous vaccine. The history is as follows: Mr. O. C., aged fifty years, lawyer, was admitted to the German Hospital December 14, 1909. He was the patient of your President, Dr. J. C. Wilson, who asked me to see Mr. C. with him in relation to a large subperiosteal collection in the left parietal region of the skull. There was nothing of note in his family history except that several children died of tuberculosis. He himself had been healthy, never having had a serious illness until August, 1909, while living at Ocean City, N. J. His first symptoms were a series of furuncles covering a period of two weeks. He went to bed September 9th, and for five weeks was treated for typhoid fever. During the latter part of his illness he suffered from a severe cystitis. He returned to his occupation early in November. In a few days he developed a severe pain in the left side of his head, above the ear and behind the position of the parietal eminence. The pain, at first dull, but continuous, progressively grew worse. About the middle of November he was compelled to return to bed, and had remained there until his admission to the hospital. The patient looked anæmic and thin, showing the effects of his long illness. Blood examination showed hæmoglobin, 80 per cent.; erythrocytes, 4,230,000; leucocytes, 10,500; with 58 per cent. of polymorphonuclear neutrophiles. The urine showed a faint trace of albumin, but was otherwise negative. Over the left parietal eminence was a large fluctuating fluid tumor evidently containing pus. This was incised, and the pus evacuated. From the pus, staphylococcus aureus was recovered in pure culture. A blood culture also showed the presence of this organism in the blood. A vaccine was made from the organism found in the abscess and four doses were given at intervals of four days. The first dose was 50,000,000, the second, 100,000,000, and the last two 150,000,000 each. There was no constitutional reaction, but the local condition improved with marked rapidity. The discharge quickly changed from pus to a clear, thick serum with an orange tinge. He began at once to improve generally; regained his appetite, gained in weight, and expressed himself as feeling decidedly better. As the bone at the bottom of the abscess was denuded and dead, he was advised to return home and report in a month, so that a sequestrum could have time to form.

He reported again on February 3, 1910, and it was then decided to remove the dead bone. The pus from the sinus still showed staphylococcus aureus. His blood-count showed leucocytes, 6,350; polynuclears, 57 per cent. A horse-shoe incision was made through the scalp, and the area of necrosis exposed. A sequestrum about as large as a dollar was removed and the rough edges of the bone smoothed off with a bone-cutting forceps. A large mass of exuberant granulations was curetted away from the dura mater. The dura was tightly adherent to the skull, so that the area of infection was sharply localized. The wound was sewed up and drainage supplied by a rubber tube coming out of the original incision. The patient was again given three injections of autogenous vaccine at four days' interval, each dose being 150,000,000. He continued to improve, regained weight, and left for home in about three weeks, in better health, he said, than he had been for years.

It is open to serious doubt whether this patient was really suffering from typhoid fever during the period of the continued fever which was so diagnosed. While furunculosis is by no means uncommon during typhoid, especially during the period of exhaustion in the later stages, it is noteworthy that the furunculosis in this case antedated the so-called typhoid by about two weeks; also that the man did not get well, but continued to suffer from an infection with staphylococcus aureus, the organism being found in the blood at the end of four months' continuous illness of alternating severity. While we cannot positively affirm that the initial illness was not typhoid fever, the history and course warrant the belief that the case was one of chronic bacteræmia. Such cases do not constitute a new observation, but it appears timely to call attention to their occurrence and to advocate the taking of a blood-culture, if not in all cases, at least in those which display atypical and long-continued symptoms, especially if pyogenic lesions be present. Particular interest, however, attaches to the rapidity of recovery under the administration of an autogenous vaccine.

Sir William Gowers has remarked that "you cannot gain any real knowledge that has not far wider application than is at first apparent." No better example of the truth of this statement can be found than in the application of vaccine therapy to the cure of disease. Twenty-five years ago, when Metchnikoff was making his initial observations of phagocytosis, and formulating his well-known ideas of immunity to bacterial invasion, who could have foretold that the factors which govern to a large extent the exercise of the phagocytic action would later be laid bare and seized upon as an aid in ridding our patients from infections? Much patient labor and many workers deserve credit for this advance, but it is beyond my scope to trace the development of the subject, ending at the present time with Wright, who deserves the greatest credit for having introduced a method of utilizing the principles upon a practical basis.

The successful use of vaccines depends upon a comprehension of the method of action and intelligent administration. It is important to realize that a vaccine is not an antitoxin and that it has no bactericidal or bacteriolytic action; in other words, it offers no passive immunity to the patient, such as is

conferred by antitetanic or antidiphtheritic sera. For its effects it depends upon the reaction of the body against the organisms injected. This presupposes that the individual still has resisting power and that a certain amount of time may safely elapse before its effects may be expected. These requirements remove from the scope of this treatment those severe fulminating infectious states in which the patient is overwhelmed by the toxins and dies in a few hours, or at the most within several days. In such cases there is neither ability to react nor time for reaction to occur. It is clear that the more severe the infection, the smaller should be the dose and the greater the caution that should be exercised. This is the exact opposite of the rule in applying curative sera which directly antagonize bacteria or their products. The reason for the caution is twofold: first, we must be careful not to add to a severe toxæmia the last straw that breaks the camel's back in our dose of killed bacteria; second, there is danger, in theory, at least, of producing too great reaction and phagocytic destruction of bacteria with liberation of a lethal dose of endotoxins. In general infections where the struggle between bodily resistance and invading bacteria is more evenly balanced there is a definite field for this form of treatment. Apparently the bodily reaction is not sufficiently provoked by certain smouldering infections to enable the patient to throw off the disease. Under the stimulus of added infectious products, in the form of a vaccine, a sharp reaction occurs, which is sufficient to annihilate the invaders. Such cases have been reported by Barr, Bell and Douglas, who were the first to apply this form of treatment in a case of streptococcic endocarditis, in 1907, by Thompson and Hoobler in this country, and by Pfeiffer and Da Costa working in connection with the German Hospital, one of the most interesting of their cases being that which I am reporting herewith. The use of vaccines in these subacute general infections constitutes the most important recent advance in this field. To secure the best results the vaccine should be autogenous, a fact which is not strange to the bacteriologist who realizes the number of strains which may be encountered in the same group of bacteria the response to which on the part of the body is highly specific. The best results are also to be expected in pyogenic infections, where nature constantly demonstrates the importance of phagocytosis by a leucocytosis and collection of pus cells. Infections with the streptococcus and pyogenic staphylococci have given the most constantly favorable results, and especially is this true of localized infections, such as carbuncle, furunculosis, acne vulgaris, persistent sinuses, etc., in which the utility of this method of treatment is beyond question.

In addition to these typically pyogenic infections, other infectious conditions have been treated with success. Gonorrhœal arthritis and pneumococcic, typhoidal and colon bacillus infections have on occasions yielded in a remarkable manner to vaccine treatment. It is as yet too early to define definitely the entire field and limits of vaccines. The important point is that they have established a footing and will remain as an addition to curative measures. They are distinctly an addition, an adjunct, and have not come to replace or supersede any well-tried forms of treatment. Neither the usual medical or surgical measures can be discontinued in favor of the vaccine. Without such

measures vaccine treatment will often fail. With them it will contribute to a more rapid, sure and complete recovery from many infectious conditions.

There is one aspect of this question to which attention has recently been directed and which is so well exemplified by this case as to be worthy of comment. This is the stimulating effect upon general metabolism which has sometimes followed vaccine treatment. The general improvement which sometimes occurs in debilitated conditions following a boil, carbuncle or other infective condition has been remarked even by the laity. It is not improbable that the response to the artificial and controllable infection represented by a bacterial vaccine may transcend the simple object aimed at and promote the general functions and well-being. Begg[1] reports a case of staphylococcus aureus infection of the leg in which during treatment by autogenous vaccine there was observed a great amelioration of a chronic bronchial catarrh which had been attended by a constant cough and profuse expectoration. He remarks that he was struck by the improvement in the general health of his patients under treatment and that they seemed to experience an increased sense of well-being as immunization advanced. Other observers have reported marked improvement in the general health of tuberculous cases after receiving vaccine treatment for an intercurrent pyogenic infection. It is possible, however, that here the effect was due rather to a heightened resistance to secondary pyogenic infection of the lungs, which plays such an important part in the later stages of tuberculosis, than to its general stimulating action. Bruce[2] has reported a number of cases of extreme neurasthenia and even mania, which he believed to be due to failure of nutrition, which he treated with polyvalent streptococcus vaccines. Of 8 chronic cases 2 entirely recovered. He was impressed with the apparent stimulation of nutrition, as 8 out of the 11 cases markedly increased in weight. In the case here reported there was a marked and rapid gain in weight and strength, following a long period of debility. I am not unmindful of the great psychic effect which a new and spectacular form of treatment may have had on many of the cases reported, though in this case there seemed to be but little opportunity for the factor. Neither do I forget the caution contained in the remark of a wise clinician regarding a new remedy, that "we must hasten to use this drug while it is still curing," but I believe I have seen not only in this but also in other cases unmistakable evidences of this beneficial general effect, and it seems to me worthy the consideration of a society devoted to therapeutics.

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1 British Medical Journal, January 22, 1910.

2 British Medical Journal, February 19, 1910.

# THE ROUTINE USE OF THE AUTOGENOUS VACCINES (BACTERINS) IN THE GERMAN HOSPITAL, PHILADELPHIA.

By J. C. Da COSTA, Jr., M.D.,

PHILADELPHIA.

The report embraced 50 cases, 17 of which were classed as septicæmia and 33 as local suppurative lesions, and suggested the following conclusions as to the utility of vaccine therapy in bacterial infections: 1. Autovaccines are of distinct service in the treatment of general septicæmia, especially in post-operative cases in which surgical measures have been ineffectual. Vaccines are useless in combating a sepsis so intense as to stifle resistance, and in such instances the clinical severity of the infection, rather than the identity of the offending bacteria, is the criterion of prognosis. 2. From the laboratory viewpoint, the prognosis is better in toxæmias than in proven bacteræmias, and the outlook is hopeless when streptococci invade the circulating blood. 3. Autovaccines produce the best results in local infectious lesions. 4. In the class of infections under consideration autogenous emulsions should be used invariably, except when some acute emergency calls for the immediate use of a stock preparation, in the meager hope of tiding over a crisis. 5. The opsonic index cannot be relied upon as an indicator for inoculation and re-inoculation, which should be governed by the general condition and local signs. 6. The best results follow a moderate initial dose of vaccine, with subsequent doses of greater potency and intervals of from three to seven days between the inoculations. 7. The larger one's experience with inoculation work, the more keenly must one realize how imperfectly the true scope and limitations of vaccine therapy are understood.

# SOME POINTS IN BACTERIAL THERAPY.

By F. E. STEWART, Ph.G., M.D.,

GERMANTOWN, PA.

In carrying out the Working Bulletin System in connection with the scientific department of a large manufacturing house during the last two years, I have accumulated in my files about ten thousand letters from physicians in all parts of the United States and our insular possessions, who have applied to us for information on the subject of bacterial vaccines and tuberculins. This paper is in the main composed of questions from such correspondents and reports of their experience in the use of these products. The questions are important ones, and the experiences reported are very suggestive in character. This paper is presented with the hope that it may excite discussion, and that the information thus derived may prove of service to the profession, particularly to those who are making a special study of bacterial therapy.

1. What nomenclature should be adopted for bacterial vaccines? The name "bacterial vaccine" was applied to this class of products by Wright because they are used for producing immunity against pathogenic bacteria similar to the immunity against small-pox produced by the use of bovine vaccines. But the name "bacterin" has been proposed as more appropriate than "vaccine," because the latter term refers more properly to Jennerian vaccination. In this paper I have used the term "bacterin" as synonymous with "bacterial vaccine," with the distinct understanding on my part that this name is free to science and commerce and is not controlled by any manufacturing house. In fact, the name was proposed to me by Dr. S. Solis Cohen,[1] of Philadelphia, who will corroborate this statement.

2. What is the diagnostic value of tuberculin reactions in tuberculosis? Several articles have appeared condemning the tuberculin diagnostic reactions as of little value, because reactions occur in persons not suffering with any active tuberculous infection. It is, however, pointed out that a large proportion of healthy individuals carry latent tubercle bacilli in their tissues, causing them to react to the tuberculin test. This fact, while, of course, well known to students of the subject, is not so well understood by the profession at large. Referring to the von Pirquet reaction, Hamburger,[2] in 1898, pointed out the fact that it is extremely difficult to find an adult entirely free from tuberculosis, and this explains the great frequency of the von Pirquet reaction in adults. And von Pirquet himself has often stated that its greatest value is in the diagnosis of tuberculosis in children. The same objection is made to the Moro reaction, although it was claimed by Emmerich,[3] and others that with the

[1] Professor of Clinical Medicine, Jefferson Medical College, Philadelphia, Pa.

[2] Münchener medizinische Wochenschrift, 1908, No. 23.

[3] Münchener medizinische Wochenschrift, 1908, No. 20.

Moro test fewer reactions occur in persons who are clinically tuberculosis-free than when the von Pirquet reaction is employed. Out of 60 cases clinically free from tuberculosis, 44 reacted to the von Pirquet test and only 19 to the Moro reaction. Drs. Charles L. Greene and Frank E. Burch,[4] of St. Paul, have given an account of the practical utility of the cutaneous and ophthalmic tuberculin tests, based upon their experiences in 83 cases, all of whom were over eight years of age. The authors conclude that the reactions were comparable to that of the old injection test with tuberculin; that the two tests ran parallel; that both tests were accurate, but the subcutaneous test the more reliable; that all patients with tuberculosis react; that advanced cases with a low resisting power give a slight reaction; that a failure to react was of great clinical importance; that the reported bad results following the ophthalmic test indicated the necessity for caution in its application and that relatively few persons react who do not on careful examination show tuberculosis.

Several interesting cases have been reported to me personally of reactions following the ophthalmic test in apparently healthy individuals. One case was that of a physician who telephoned to me from a distant city, where he has a large private practice and a private sanatorium devoted to the treatment of tubercular disease. To assure a patient of the harmlessness of the conjunctival test he used it in his own eye, when to his horror a reaction occurred. In great alarm he telephoned to the writer for advice, which advice was to come to Philadelphia, for a careful physical examination. Dr. S. Solis Cohen examined the case with me. We found that the patient was overworked; that his general health was giving way under the strain; that he had a limited area of slight dullness in one of his lungs, and that several members of his family had died of tuberculosis. Under these circumstances we assured him that, although he had no symptoms justifying a diagnosis of acute tuberculosis, the probabilities were in favor of his rapid decline and death if he did not at once drop his practice for a time and take proper rest and treatment. He went away sorrowful, as he felt that he could not afford to take such advice, but, being convinced as to its wisdom, he did finally follow it. Six months later he reported to me at the Atlantic City meeting of the American Medical Association. He had completely regained his health, had added materially to his weight, and had returned to his work. This case illustrates another phase of the subject to which the various authorities have not called any special attention: that is, the value of the tuberculin reaction in diagnosing doubtful cases. The physician just mentioned said that if the reaction had not occurred he could not have been convinced of the necessity for making such a sacrifice in order to regain his health, and that he would doubtless have continued at work until forced to stop, when it might have been too late. These tuberculin reactions are therefore of great service to the physician in convincing doubtful patients and their friends of the necessity for proper treatment, and the fact that those who are apparently well sometimes react to the tuberculin does not in the least militate against the value of the test; it merely proves the presence of latent tubercular lesions.

[4] New York Medical Journal, June 20, 1908.

Drs. Samuel McC. Hamill, Howard Childs Carpenter and Thomas A. Cope,[5] of Philadelphia, reported the results obtained in 134 cases in children under eight years of age. They found uniformity of reaction with the von Pirquet, the Moro, and the ophthalmic reactions, but considered that all three were of less value in the diagnosis of the irregular forms of tuberculosis than had been hoped that they would be; they considered a negative reaction of more value than a positive one; that the type of the reaction bore no relation to the type of the disease, and that the ophthalmoreaction was sometimes followed by serious inflammation of the eye, and even by loss of vision. Nothing has been published in 1909 or 1910 to alter to any great degree the verdicts published in 1908. The ophthalmoreaction has been quite generally abandoned, on account of the danger attending its use, yet, in the hands of Baldwin,[6] of Saranac, results seem to be uniformly good. Baldwin uses a ½ of 1 per cent. solution of precipitated tuberculin, repeated if no reaction occurs, using a 1 per cent. solution in the other eye. He takes care to confine the test to healthy eyes, and calls attention to the danger of using it in inflamed or diseased eyes.

3. What is the value of typhobacterin, or typhoid vaccine, as an immunizing and curative agent? The value of the injection of killed typhoid bacilli in immunizing armies is now generally recognized by most civilized nations, but its use by individuals about to visit regions infected with typhoid fever is perhaps a novelty. In a recent conversation with a former representative of the United States Consular Service in China, who was about to visit India, I learned, much to my surprise, that well-informed laymen now consider it a wise precaution for persons to take immunizing doses of typho-bacterin before going to typhoid-infested regions. I learned also, more recently, from a New England correspondent that the lay public is beginning to demand bacterial treatment from physicians for other diseases besides typhoid fever.

Reports regarding the curative value of typho-bacterin are not sufficiently conclusive to warrant dogmatic statements. The following instance, however, illustrates the possibilities of this treatment. A most interesting letter recently received from a physician contained a clinical chart showing the remarkable results obtained by him in a case of typhoid fever. On the tenth day of the disease, after a temperature record of 104° F. for seven or eight days, with a pulse rate of 140, an injection of 40,000,000 killed typhoid bacilli was given. Within forty-eight hours the temperature had returned to normal and the pulse to 76, and there was no further rise of either. I am, of course, aware that one swallow does not make a summer, and that this case may only be a remarkable coincidence. But such brilliant results are unfortunately apt to cause overenthusiasm and disaster before experience has been gained, as is shown by the following history: A physician in a certain county became very much elated on account of the remarkable results he had obtained in several cases with the bacterial treatment, and he told the good news to his professional brethren, who commenced to employ bacterial therapy without proper discrimination. Over-

[5] New York Medical Journal, June 20, 1908.

[6] Adirondack Cottage Sanitarium, Trudeau P. O., Saranac Lake, N. Y.

enthusiasm without proper precaution was followed by deserved disaster, but unfortunately the victim of his own inexperience blamed the disastrous results on bacterial therapy instead of on his errors, and contributed to the county medical society a paper which led to the passage of a resolution condemning the use of bacterial vaccines *in toto*, and it will doubtless be some time before the members of that medical society realize that the fault is not that of bacterial therapy. In the mean time, physicians and patients are the losers.

4. What is the value of Neisser bacterin, or gonococcic vaccine, as a remedy for gonorrhœal affections? It seems to be generally agreed that in the treatment of gonorrhœa the acute urethral cases do not require as large doses as do the chronic cases; also that arthritic cases require much larger doses than the urethral cases. Allen[7] "warmly recommends" the routine practice of giving to every acute urethral case one or two injections of from 75,000,000 to 150,000,000 gonococci as soon as the more acute symptoms begin to subside and the thick discharge to diminish. Allen states that convalescence was complete in two or three weeks, and that no secondary complications or backward extension occurred in any of the series of cases treated in this manner. Other authorities prefer much smaller doses in acute cases. One of my correspondents, Dr. W. R. Jamieson, President of the International Medical Association of Mexico, writes as follows: "I may say that I am having most excellent results with the Neisser bacterin, more especially since I have learned, mostly by bitter experience, to use it properly."

In a paper read before the fifth annual meeting of that association, at Aguascalientes, January 24 to 27, 1910, Dr. Jamieson recommended in acute cases doses of 5,000,000 to 15,000,000 at intervals of two to four days, according to the stage and severity of the disease, gradually increasing the dose as the symptoms abated, and taking pains to avoid, as far as possible, the production of a too pronounced negative phase. The chronic cases received an initial dose of 25,000,000 to 50,000,000, repeated in five to eight days. (See Therapeutic Gazette, May 15, 1910.)

5. What is the value of Neisser bacterin as a diagnostic agent? Irons[8] states that the injection of 500,000,000 killed gonococci into the tissues of a person free from gonococcal infection was found to cause practically no constitutional disturbances in 8 cases. In infected cases, however, results were quite different. Within twenty-four hours, and corresponding to the negative phase, there was increased articular pain, tenderness, rise in temperature, and general malaise; the reaction being so pronounced that it was suggested that the injection of killed gonococci be employed as a diagnostic agent in cases of doubtful gonococcic infection. It has been my fortune to learn the practical bearing of this test in several cases. A Philadelphia physician was called to treat a patient who had been discharged from a hospital after several weeks' treatment of what was pronounced to be tuberculous infection of both knee-joints. The hospital treatment having been of no benefit, the doctor tested the

[7] R. W. Allen, M.D., B.S. Lond., late pathologist to the Royal Eye Hospital; late Gull student of pathology, Guy's Hospital.

[8] Archives of Internal Medicine, vol. i, No. 4, p. 433.

case with tuberculin, with negative results. A dose of 50,000,000 killed gonococci was then injected, against which there was a violent reaction, followed later by marked improvement in the condition of the patient. Failure of reaction after injection of the dose used by Irons is not to be considered sufficient to justify the physician in pronouncing a case non-gonorrhœal, as the following incident shows. A classmate of the writer, a well-known Philadelphia surgeon, telephoned that he was at a loss how to proceed in a case of gonorrhœal arthritis, in which doses of 300,000,000 killed gonococci had been of no benefit, although he had used this amount successfully in other cases. I advised that the dose be gradually increased until he obtained a reaction, and then continue the treatment in doses just below the reaction point. This patient was at first given doses of 50,000,000 killed gonococci, with slight reaction. The dose was then increased to 500,000,000. No reaction occurred, but there was some apparent diminution of the discharge. Next day a dose of 1,000,000,000 was given without result of any kind, and two days later the same amount was again injected, without reaction, but with further decrease in the discharge. The next day a dose of 1,500,000,000 was given, and three days later the dose was increased to 2,000,000,000. The next day a dose of 1,000,000,000 was given, and two days afterward 1,500,000,000. Owing to indiscretion on the part of the patient a relapse then occurred. Four days elapsed before the next injection of 1,500,000,000; then, two days later, a dose of 3,000,000,000 was injected. During all this time the patient was gradually improving, but no further reaction occurred, although the dose had been greatly increased. The patient was under observation from February 9th to April 25th. He was given in all 33 injections, increasing from 50,000,000 to 3,000,000,000 at a single dose, no reactions being observed in the larger doses.

In the opinion of this observer the initial doses of Neisser bacterin should be larger than usually employed and large doses should be used to keep up the effect, and that in this manner the time consumed in the treatment of the patient would be shortened.

Other physicians report better results in small doses than obtained by them in larger doses, which goes to show that each case must be individually considered, and the doses, as to amounts and interspacing, guided by the condition of the patient.

6. What is the value of acnebacterin, staphylobacterin, and staphyloacnebacterin as therapeutic agents? Acnebacterin is said to give better results in the treatment of comedones than the staphylobacterin, while the latter appears to be preferred in acne indurata. Staphyloacnebacterin seems to give good results in acne of either type. Large and progressively increasing doses are often required, with persistent treatment for months. Allen recommends an initial dose of 250,000,000 killed staphylococci, soon increasing to 500,000,000, 750,000,000, and 1,700,000,000. The interval between doses varies from three days to a week or more. He reports a case which required a dosage of 4,000,000,000, at ten-day intervals. He also states that in cases of deep-seated foci which refuse to come to a head (acne indurata) hyperæmia by means of dry cupping is a very useful adjuvant to treat-

ment with bacterial vaccines. Many cases of acne do well under treatment with mixed stock vaccines—albus, aureus, and citreus. Other cases apparently require treatment with autogenous vaccines. I have received many requests for information as to the bacterial treatment of acne, which are invariably answered by advising that the Working Bulletins be carefully read, after thoroughly studying Wright's original papers and learning the principles of vaccine therapy as described by the master thereof. Attention is called to the necessity of using with the bacterin treatment the same treatment as would be employed without bacterial vaccines. Especial emphasis is laid on the fact that Wright recommends the production of hyperæmia in connection with the use of bacterial vaccines. Many cases of acne are cured by bacterial therapy, but others have proved very stubborn. Treatment with combined staphylococcic vaccine has proved quite successful in the treatment of chronic furunculosis. Some physicians prefer to use the staphyloaureus vaccine, as it is said that the greater proportion of the cases of acne are due to aureus infection. The fact that staphylostreptococcic mixed infection occurs should not be forgotten.

After reading this paper before the American Therapeutic Society it was my privilege to confer with Dr. Martin F. Engman, of St. Louis. He reported his experience in the treatment of 500 cases of acne with acnebacterin in a paper read before the American Dermatological Society, Washington meeting, and emphasized in our interview what he had reported in his paper, viz.: in his experience better results are obtained in doses of 1,000,000 to 5,000,000 killed bacteria than in the larger doses recommended by other observers.

7. Is stock streptococcus vaccine, or streptobacterin, of any therapeutic value? It is, of course, recognized that the streptococcus is not a single individual, this being the generic name for a large and heterogenous class, the members of which are capable of producing the most varied forms of lesions. Yet, in spite of the frequent failures of bacterial therapy in streptococcic infections, excellent results are often obtained from treatment with stock vaccines. A Philadelphia physician, with whom I have several times been in consultation, recently asked me for suggestions as to the treatment of a case of erysipelas involving the face, head and ear. The patient complained of headache and the temperature was 103° F. Bearing in mind what Dr. Barton C. Hirst,[9] of Philadelphia, had told me of his experience in the treatment of streptococcic infection, using both antistreptococcic serum and streptobacterin, and being of the opinion that the use of the bacterin increases the efficacy of the serum, I suggested the injection of streptobacterin, to be followed by the use of the antistreptococcic serum, if necessary. Soon after the injection of the bacterin the temperature began to fall, and within twenty-four hours it registered 100° F. Another injection of bacterin was given, and within a few hours the temperature returned to normal, the eruption meanwhile fading away. As to the combined treatment with serum and bacterin, during the past year there have been reported to me no less than six cases of streptococcic infection in which antistreptococcic serum proved curative. The doses of 80 cubic centimeters, three or

[9] Professor of Obstetrics, University of Pennsylvania, Philadelphia, Pa.

four times during the twenty-four hours, employed by Dr. Hirst may seem excessive, but are necessary to secure the desired results. If this dosage can be reduced by combining streptobacterin with the serum it will be very advantageous from the standpoint of economy, if for no other reason. Still greater advantages are to be obtained by using the bacterin first, as it may be found to be sufficient. It is, of course, necessary that a polyvalent bacterin or a polyvalent serum be employed, and, for reasons stated, one brand may prove efficacious and another one fail, as occurred in a case in which Dr. Hirst was called as consultant.

Theoretically, autogenous vaccines should always be used in the treatment of streptococcic infections, but this is not always necessary, as is shown by the experience of the Russian physician, Gabritschewsky, who reports good results with stock streptococcic vaccine as a preventive and curative in scarlet fever. His observations were made on more than seven hundred children.[10]

8. Of what value is streptobacterin as an immunizing agent? It is believed by some physicians that streptobacterin may possess great value as an immunizing agent in prophylaxis against streptococcic infections. This claim is now being tested in the following manner: All the children in a certain school where 2 cases of scarlet fever had recently appeared have been treated by giving to each child a dose of bacterin of 10,000,000 killed streptococci, it being hoped in this way to produce immunity and prevent an epidemic. The result of this treatment is being watched with much interest.

9. Is neoformans vaccine, or neoformans bacterin, a cure for cancer? Several years ago Doyen, the French surgeon, isolated from new growths a micrococcus which he believed to be the specific cause of cancer. The work of other investigators seemed to disprove that this micrococcus is the cause of cancer itself, but many believe that the intercurrent infections are frequently caused by the micrococcus neoformans, which is found in a large proportion of malignant new growths, especially those which are ulcerated. Wright and others have used neoformans vaccines in the treatment of ulcerated cancerous conditions, sometimes with remarkably beneficial results. Doyen is now using in Paris a treatment the nature of which he does not divulge in full, but it is supposed that neoformans vaccine is one of the products he employs. A Baltimore physician who spent some months with Doyen reports that he is convinced that the latter is obtaining good results, but he calls attention to the fact that Doyen uses fulguration before employing bacterial therapy and that this is intended to prevent metastasis. Some reports received from physicians who are using neoformans vaccine in the treatment of inoperable cases state that it often removes the odor and makes the patient more comfortable.

10. What is the therapeutic value of pneumococcic vaccine, or pneumobacterin? Much interest is being aroused by collective investigation of

[10] For his extensive researches and confirmatory reports, you are referred to Roussky Vratch, 1905; Centrlbl. f. Bakt., vol. xli, 1906, pp. 719, 844; Zlatogoroff, *ibid.*, vol. xlii, 1906, pp. 77, 156; Langoway, *ibid.*, pp. 362, 463; Nidrigailow, *ibid.*, pp. 13, 102. See also editorial entitled "The Treatment and Prevention of Scarlet Fever by Injections of Dead Streptococci," Journal of the American Medical Association, January 4, 1908, p. 43.

pneumonobacterin in the treatment of lobar pneumonia. Dr. Timothy Leary[11] calls especial attention to the following points: early diagnosis, early administration of the bacterin, and the necessity of full doses, that is, 10,000,000 to 50,000,000, progressively increased in acute cases, every four to eight hours. We were recently informed, however, that Dr. Leary has lately changed his dosage from the foregoing to 100,000,000 once in the twenty-four hours. It has been stated as an objection to this treatment that bacterial vaccines are not indicated in acute conditions, but Harris,[12] Willcox and Morgan,[13] MacDonald,[14] Martyn,[15] Batten,[16] and others, as well as Leary, are using the vaccine in acute conditions, with apparently beneficial results. Interest has been excited among the dentists by Goadby's[17] articles on the "Vaccine Treatment of Pyorrhœa Alveolaris." He treated 47 cases, 36 of which were cured, and 9 relieved. Leary,[18] in an article on the bacteriology of pyorrhœa alveolaris, states that he has studied about 100 cases of pyorrhœa, in which he found a great variety of organisms, his most constant finding being the pneumococcus. Medalia[19] finds that 90 per cent. of his cases of pyorrhœa alveolaris are of pneumonococcic infection, with which the staphylococci and the streptococci are more frequently associated than any other organisms. He also reports good results from the bacterial treatment of such infections. Sufficient evidence has not yet been accumulated to warrant a verdict either in favor of or against this method of treating pyorrhœa, but it is hoped that a remedy has at last been found for this most obstinate affection.

11. What are the causes of failure in bacterial therapy? The following are some of the possible causes of failure in bacterial therapy:—

(*a*) *Unrecognized Identity of the Infecting Bacteria.*—One of the most important factors in bacterial therapy is to know the identity of the infecting germ. This can be demonstrated by examination of the tissues or fluids of the infected zone, but many physicians in the country and the smaller towns are not sufficiently posted in bacteriology to do this work or to recognize the identity of the infecting germ, and, rather than put patients who cannot afford it to the expense of going to some medical center for a diagnosis, they do the best they can under the circumstances, and inject a stock bacterial vaccine of the kind they have reason to believe is the proper one to use. That a certain proportion of such cases fails is not surprising.

(*b*) *Unrecognized Mixed Infection.*—One correspondent used Neisserbacterin in a case of cystitis of supposedly gonococcic origin, but without improvement in the patient's condition. A bacteriological examination revealed

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11 Boston Medical and Surgical Journal, November 11, 1909.
12 British Medical Journal, June 26, 1909.
13 Lancet, 1909, vol. ii, p. 471.
14 Pathological Society, London, January 17, 1905.
15 Southern California Practitioner, 1908, p. 162.
16 Lancet, 1909, vol. i, p. 1454.
17 Lancet, 1909, vol. i, p. 1875.
18 Dental Cosmos, 1910, vol. lii, p. 52.
19 Boston Medical and Surgical Journal, 1910, vol. clxii, p. 42.

the presence of colon bacilli, and coli-bacterin was then used. This was followed by much improvement, but, as a cure did not result, another examination was made. This demonstrated the presence of gonococci in abundance; so treatment with the Neisser-bacterin was resumed, and complete recovery followed. Acne bacilli and staphylococci are frequently associated in acne; in bronchopneumonia pneumococci and staphylococci are generally present; staphylococci, streptococci, and other germs exist at the same time in tuberculosis, and mixed infection is said to be the cause of death in most cases. Friedlander's bacillus, micrococcus catarrhalis, staphylococci, etc., are found together in catarrhal affections. Mixed infection often requires a mixed bacterin treatment, and cases unsuccessfully treated with stock vaccines should not be pronounced failures until autogenous vaccines have been used.

(*c*) *Failure to Bring the Blood, with its Opsonin, in Contact with the Invading Micro-organisms.*—Wright[20] calls attention to the fact that failure may result if the blood, with its opsonin, resulting from the injection of bacterial vaccines, is not brought to the area of infection. For this purpose he recommends rubefacients, massage, Bier's method of hyperæmia, exercise, etc. The importance of following this advice of Wright is shown in the case of gonorrhœal arthritis of both knees previously mentioned in connection with the use of Neisser-bacterin as a diagnostic agent. This case was of several months' duration, and at once on the employment of the Neisser-reaction therapeutically there was very marked improvement. The improvement had ceased, however, and I was asked to see the case in consultation. As I found that the attending physician was provided with apparatus for producing hyperæmia by the local application of heat, I advised its use. The physician employed the electric light bath, and obtained excellent results from its use, together with continued treatment with the bacterin.

(*d*) *Failure to Recognize that Bacterial Vaccines are Vegetable Drugs Differing Widely in Properties and Potency and Each Requiring Separate Consideration as to Method of Application and Dosage.*—The difference between bacterial drugs in regard to properties and potency is well illustrated by tuberculin and Neisser-bacterin. The initial dose of tuberculin R. is .0001 milligram, gradually increased for effect, and unless great care is used dangerous reactions occur. The initial dose of Neisser bacterin varies from 20,000,000 to 3,000,000,000 and the reactions produced are comparatively mild. Both of these products vary widely in potency; which suggests the next reason why bacterial therapy sometimes fails.

(*e*) *Want of Standardization.*—Bacterial vaccines, like other vegetable drugs, require standardization to assure uniformity in character, quality and strength. This necessity is well illustrated by Neisser-bacterin. Injections of 50,000,000 produce marked reactions in some cases, while in other cases doses of 3,000,000,000 or more may be administered before reactions occur. This wide range of dosage is to be accounted for either by the difference in the sensitiveness of the body-cells of the individual to stimulation, or by difference

[20] Barton Lisle Wright, M.D., Surgeon, U. S. Navy.

in the potency of the bacterin. Now, when it is considered that the tinctures of strophanthus on the market vary 6000 per cent. in potency, and that no two lots sent out are the same in strength unless standardized, the question is at once suggested, does not the same necessity for securing uniformity of products exist in relation to bacterial vaccines? Standardization by counting the number of killed germs per cubic centimeter is not sufficient, because the virulency of each bacterial culture is different. Standardization by weighing the amount of bacterial substance present is no better than standardizing a tincture or fluidextract by weighing the amount of extractive it contains. Standardization in either case requires the determination by chemical assay or physiological test of the amount of activity the product possesses. There are no reliable methods for standardizing bacterial vaccines and tuberculins.

12. What are combined bacterial vaccines, or combined bacterins? Combined vaccines, or combined bacterins, are mixtures of two or three kinds of pathogenic bacteria usually found associated in mixed infections. Staphylobacterin, as usually furnished, is a combination of the three species of staphylococci, viz., albus, aureus and citreus. Staphyloacnebacterin is a mixture made by adding the acne bacilli to staphylobacterin. In regard to the use of combined vaccines Allen says: "In certain conditions, such as pulmonary phthisis, tuberculosis of the bladder and kidneys and bones and joints, additional gravity is added to the case when to the primary infection secondary ones are added. All are familiar with the ease with which a case of early pulmonary phthisis or tubercular joint disease yields to appropriate treatment, and the difficulty of dealing with such a case when once staphylococci or streptococci have complicated the infection. Occasionally, it is true, great improvement follows the administration of tuberculin alone, but the best results will, I am convinced, be secured by either previously or simultaneously attacking the secondary infection. In these instances it is, as a rule, easy to ascertain the exact nature of this infection. In bladders and kidneys it is usually the bacillus coli communis; in bones and joints, staphylococci or streptococci. Other forms of bacillary infection there are, however, such as pyorrhœa alveolaris, gleet, and chronic tracheal catarrh, in which it is well-nigh impossible to tell which out of the many different bacteria present are responsible for the condition. The only thing then to do is to employ a 'combined vaccine.' " A correspondent recently called attention to the work of Dr. P. J. Pothuisje, of Denver, who is using pneumobacterin in conjunction with tuberculin in the treatment of pulmonary tuberculosis. With patients whose temperature is so high that tuberculin is contraindicated, he uses pneumobacterin only, and in most cases this causes the temperature to decline, the cough to lessen, the weight to increase, and the general condition to improve; so that, after a short period of this treatment, he is able to begin treatment with the tuberculin.

13. What is a polyvalent vaccine or bacterin? Bacterial vaccines are said to be polyvalent (of many worths) when made from cultures containing a number of varieties of the same kind of bacteria. Streptobacterin is a polyvalent vaccine made from a culture of streptococci which contains a large variety of streptococci.

14. Are bacterial vaccines harmless? The statement is sometimes made that bacterial vaccines are perfectly harmless. As a general statement, it is safe to say that drugs which are "perfectly harmless" are perfectly useless. Bacterial vaccines, or bacterins, consist of killed pathogenic bacteria and their toxins. They are therefore toxins, not antitoxins or curative sera, with which they are frequently confounded by physicans unfamiliar with bacterial therapy. When the disease germs in any given infection are not causing sufficient stimulation of the body-cells to generate enough specific opsonins and other antibodies to effect a cure, the use of bacterial vaccines will often prove of great therapeutic value. If, however, an overdose is given, the injection is followed by a marked exacerbation of symptoms, due to a pronounced negative phase, which may continue if the doses given are excessive or too frequently repeated. According to Wright, if a proper dose of vaccine has been injected, no clinical symptoms should be produced, even during the negative phase; but other authorities advocate the injection of doses large enough to produce a slight clinical reaction, manifested by a feeling of malaise, slight rise in temperature, etc., and no doubt there are times when it is proper to increase the dose until a slight reaction does occur, at least for the purpose of testing the activity of the vaccine. The time to repeat the injection is during the positive phase, which is clinically characterized by improvement in the condition of the patient. Generally speaking, the intervals between doses should be from three to five days, to be increased to intervals of a week or two, as indicated, as the treatment progresses. Sometimes in acute conditions the injection may be repeated to advantage every twenty-four hours, and as the patient improves the intervals may be lengthened and the dose possibly increased. Used with proper precautions and in properly selected cases, it may be stated that bacterial vaccines are harmless, because when thus employed they not only do no harm, but are distinctly curative in their action. When they are used without discretion, however, they are capable of doing harm, although fortunately the harm is slight and no serious results are to be apprehended. This statement, it should be said, does not apply with equal force to all bacterial vaccines. Among the bacterial vaccines or bacterins to which it does not apply are the newer tuberculins, namely: "Tuberculin R." and "Bacillen Emulsion," the indiscriminate use of which is sure to be followed by disaster. The same statement applies to "Old Tuberculin," but this product being a glycerin extract of tubercle bacilli, and not containing the germ bodies, is not classed as a bacterin. Moreover, in the present state of knowledge concerning bacterial vaccines, the physician who limits himself to fixed rules of dosage is bound to lose out.

15. What are the keeping properties of bacterial vaccines and tuberculins? In preparing bacterial vaccines Wright uses a temperature of 60° C. for one hour, to kill the bacteria. It has recently been suggested that bacterial vaccines be prepared by omitting the use of heat, the ½ of 1 per cent. phenol used as a preservative being amply sufficient to kill the bacteria. It is claimed that bacterial vaccines thus prepared are more active and keep longer, but I am informed that Wright sometimes uses vaccines two years old which have been prepared by the use of heat. As regards tuberculin, it is generally sup-

posed that tuberculin "Old" keeps indefinitely, yet some observers claim that ointment made from it gradually loses its activity. However, I am informed by veterinarians that tuberculin "Old" reacts with cattle even when it is five years old, provided it is clear and odorless. The keeping power of the newer tuberculins is also in question. Serial dilutions of tuberculin, especially the higher dilutions, are said to deteriorate gradually and to be unreliable after two or three months. Some specialists renew their dilutions once a month, while others, equally experienced, use dilutions six months old. Conclusive evidence on this point is greatly needed.

Finally, I desire to call your attention again to the value of the Working Bulletin System as a method whereby manufacturers of new materia-medica products may place in the hands of the medical profession valuable information concerning these products. As stated in a former paper, some years ago I suggested the formation by the large manufacturing houses of scientific departments and the adoption by these departments of the Working Bulletin System. This suggestion was accepted by a number of the manufacturing houses, and the plan, more or less modified, was carried out by several of them. The manufacturers of materia-medica products, with their scientific departments, are certainly in position to speak with authority in regard to the products themselves, but, as they are not engaged in the practice of therapeutics, they are not in position to teach the profession how to apply these products in the treatment of the sick. The Working Bulletin System, therefore, if properly employed by manufacturing houses, will consist of the publication of information relative to the manufacture and standardization of the products, and also of abstracts from the reports of competent clinical observers, impartially selected from the medical press throughout the world; due credit being given to the authors and publishers, so that the original articles may readily be referred to. What is most urgently needed is a strong central board of control, bureau of materia medica, or pharmacologic society, to act as a clearing house, including in its membership representatives of the medical and pharmaceutical professions and the large manufacturing houses, under whose supervision the Working Bulletins would be published. This would give scientific standing to the Bulletins and would render the Working Bulletin System of great service to both professions. This I have continuously advocated for thirty years, and I am more and more convinced of the value and importance of the plan. I take pleasure in presenting to the library of the American Therapeutic Society a bound copy of Working Bulletins on Bacterial Vaccines and Tuberculins, as an example of this class of literature.

## BACTERINS: THEIR PRESENT STATUS IN THERAPEUTICS.

By NOBLE P. BARNES, M.D.,

WASHINGTON, D. C.

THE use of the bacterial vaccines now proving of therapeutic value, he said, was based upon the opsonic theory, advanced by Sir. A. E. Wright. From the mass of reports some brilliant results were found—some of doubtful value, and some of positive harm. The whole subject had been sifting through an experimental stage, of which little was known or understood; however, with increased knowledge, more exact and scientific courses could be pursued. But we were yet far from realizing the dream of the immortal Pasteur, when he said, "It is possible for man to eradicate every contagious disease from the face of the earth." One of the common causes for failure with bacterial vaccines was misapplication, namely, the attempt at active immunization when the defenses have been exhausted and a bacteriæmia exists. These were cases for antitoxins, and not for toxins. The whole subject was confused and confusing, on account of the variability in the application. Some guide their doses by the opsonic index, others on clinical signs; some are satisfied with stock preparations and others insist on autogenous bacterial vaccines. Doses, intervals, and the keenness of observation and excellence of judgment are likewise at variance.

Among the conclusions reached by B. A. Thomas in his report of 119 infections treated by vaccines were the following: "The diseases contraindicated for bacterin therapy are the diffuse infections, characterized by septicæmia, pyæmia and grave sapræmia.

"Those in which therapy by this agent is beneficial or curative are the superficial acute, subacute and chronic processes; especially the last two.

"The acute cases, in which brilliant results can be uniformly expected, are those of acne vulgaris, furunculosis, carbunculosis and subcutaneous abscesses.

"Subacute and chronic gonorrhœal and tuberculous affections are amenable to bacterial immunization, and, because of the impossibility and impracticability often of employing an autogenous bacterin, the reliable stock preparations should be used.

"Certain acute gonorrhœal infections can be benefited.

"It is questionable whether tuberculin therapy should ever be employed in very acute tuberculosis. Opinion is divided as to whether or not acute miliary tuberculosis and death supervened as a result of tuberculin therapy in one of the cases.

"The mixed infections in chronic tuberculous disease afford an important prospective field for alternating bacterial inoculations and tuberculin therapy.

"Autogenous bacterin is always to be preferred over the stock preparations, and success or failure frequently depends on this fact.

"It is believed that the best effects, therapeutically, particularly in chronic cases, occur when the quantity of bacterin is slowly and cautiously increased during successive inoculations, thereby, as has been thoroughly demonstrated in tuberculin therapy, avoiding high hypersusceptibility or anaphylaxis.

"Therapy by both bacterins and tuberculins can be satisfactorily executed by keen observance of the clinical symptomatology. Reliance on the opsonic index as a guide is not only unnecessary, but often actually conducive to erroneous conclusions, owing to its variability.

"Bacterin therapy, by virtue of its potency to do more harm than good when unskillfully managed, will or should probably not become a universal therapeutic measure in the hands of the general practitioner, unfamiliar with bacteriology or work in the laboratory. Ignorance and wantonness are incompatible with ambition and energy, and an otherwise meritorious therapeutic agent thus abused will ultimately fall into disrepute.

"Bacterins and tuberculins are not 'cure-alls,' but when intelligently used serve as invaluable aids to nature in fortifying the bodily defenses, thereby accelerating convalescence, diminishing complications and promoting cure."

The tuberculin reaction in the eye, according to Peter, has a distinct, though limited, field. Bandelier and Roepke have few words of commendation for the conjunctival test. Wolff-Eisner has made 4000 tests and asserts that a positive ocular reaction to tuberculin, with his technique, indicates an active tuberculous focus, while the cutaneous methods give positive findings even with latent foci. McNeil uses both skin and eye reaction, but rather favoring the former. The eye test is evidently more dangerous, and is contraindicated in the presence of eye affections and, if positive, speaks only for active processes that can be diagnosed by other methods. If negative, it is of no value, for it is not nearly so sensitive as the cutaneous test. The skin test is now regarded as a most valuable addition to the means of diagnosing tuberculosis.

Lowenstein reports favorably his experience with tuberculin treatment of 300 cases of open pulmonary tuberculosis. The main point he makes is to avoid introducing new toxins before the effect of the previous toxins has been thrown off. P. K. Pel says that he has been unable to acquire much enthusiasm for tuberculin therapy, and he declares that the failure to institute the treatment is not a sin of omission for the present. Burroughs says, "In my opinion tuberculin is of no value except for diagnostic purposes." Bullock says, "I have employed tuberculin extensively, but cannot find its place, if it has any, in the treatment of tuberculosis." Trudeau says, "I have no statistics to present beyond what the post-discharge mortality of patients at the sanitarium has shown, namely, that from 18 to 25 per cent. more of the treated than the untreated cases discharged from the sanitarium during the past 15 years were living at the time we made inquiry." Pottenger speaks favorably of the tuberculin treatment. "In the hands of careful men," he says, "the opsonic index will yield results." McFarland is opposed to the treatment, and bases his opposition on the fact that "no animal can be immunized against tuberculosis by any previous treatment with tuberculin, nor can any animal already tuberculous have its life considerably lengthened by tuberculin." Theodore Potter

says, "After fifteen years in the use of tuberculin to some moderate extent all the way along and more actively lately, I confess I do not know whether it is of much use or not."

Autogenous vaccines have been extensively employed with some exceptionally gratifying results. Favorable results have been reported with the vaccine treatment in infections with streptococcus erysipelatis and streptococcus rheumaticus and pyogenes aureus. Wilcox, Morgan and Leary report favorably on the use of vaccine in pneumonia.

Oastler, speaking of pelvic infections, expresses the belief that the greatest good accomplished by bacterial vaccines up to this time is in the treatment of subacute or chronic pyæmia or septicæmia; that the acute violent cases of puerperal sepsis do not respond to the bacterial vaccines. Vaccines are indicated after the acute attack where there is poor resistance, often in these turning the tide in favor of the patient; the dose is still experimental. He claims most satisfactory results with the staphylococcus aureus and bacillus coli, and less with the streptococcus. Gonococcus vaccine in gonorrhœal urethritis is disappointing. Reviewing their treatment of 97 cases of sepsis with bacterial vaccines, Hartwell, Streeter, and Greene draw the following conclusions: First, that bacterial vaccine should be further employed in puerperal infections which do not immediately respond to routine treatment; second, that bacterial vaccines are of much value in the type of sepsis which has remained stationary for some time.

The experience of the Germans with antityphoid inoculation confirms the results reported in England and the British army. As a result of these apparent successes it is proposed to introduce the same procedure into the army of the United States.

DISCUSSION.

*Dr. White* said that, in addition to tests with tuberculin, he had also made tests with gold chloride solution, and found that he obtained the same reactions with the gold solution as with tuberculin, when used hypodermatically. In his opinion the Calmette test was very unreliable. In some cases it had been found that the application of tuberculin to the mucous membrane of the eye of patients who have no tuberculous diathesis whatever has been followed by a violent reaction. This had been shown in certain instances to be due to the presence of bacteria in the eye. It had recently been shown, moreover, that this reaction does not take place in tuberculous cases when the mucous membrane of the eye has been previously thoroughly sterilized and the tuberculin is applied. Hence, when the tuberculin test was to be made, the eye should first be thoroughly sterilized in order to do away with all lurking germs in the conjunctiva, and even when this precaution was taken the accuracy of the test was often questionable.

*Dr. Da Costa* said he was accustomed to insist on the use of autogenous bacterins as being in every way the most reliable. The method of preparing them was not difficult, but the details of the technique should be adhered to with great care. In reply to a question by Dr. Stewart, he said it took twenty-four hours to prepare an autogenous vaccine.

# IMMEDIATE AND AFTER MANAGEMENT OF THE PUERPERANT.

By JESSE SHOUP, M.D.,

WASHINGTON, D. C.

THE puerperant is presumed to have been prepared according to the rules of modern antiseptic procedure at the beginning of labor, in that the hair over the vulva has been either cut short or shaved; that she has had a general scrubbing bath; that the genitals particularly have been cleansed with soap and water, especial care being given to cleansing the inside of the thighs and the folds or creases of the skin, and that, following the bath, the parts, from the waist down, have been bathed with a 1:1000 solution of mercuric bichloride. Also that, during the progress of labor, the vulva was kept covered with a towel wrung out of a solution of 1:1000 bichloride, and all unnecessary internal examinations avoided. The obstetrician should train himself to secure all possible information as to the progress of labor from external examinations, palpation, auscultation and intelligent observation. When an internal examination is made, the hand should be covered with a sterile glove and the vulva separated prior to the introduction of the examining finger. A glove is not sterile if it has touched some part of the patient's clothing or the bedding prior to the examination. It is not uncommon to see the doctor put on sterile gloves and then arrange the patient. During the third stage of labor the necessity for internal examination is extremely rare, and the nurse should never be allowed to make internal examinations at any time without the direct request of the physician. The evidence derived from numerous and careful investigations favors the conclusion that the normal vagina is free from micro-organisms, and that the vaginal secretions are fatal to them, with the exception of the gonococcus. So it may be assumed to be true that all infection of the genital tract is caused by either the nurse or the doctor. It is impossible to thoroughly sterilize the vulva, no matter how carefully we try. This being the case, it is readily seen how the examining finger may carry infection from the vulva to the cervix and upper vagina, where it can easily enter the uterus or be absorbed through broken surfaces of the mucous membrane. If the accoucheur would but keep in mind the fact that there is essentially an open canal extending from the vulva through the vagina, up the uterus and through the tubes to the peritoneal cavity, he would rarely neglect the essentials of asepsis.

In cases where suitable light and assistance is at hand, all lacerations of the perineum and lower vagina should be repaired immediately after labor. If, for good reasons, this cannot be done at the time of delivery, it should be done within the twenty-four hours following. Where instruments have been used to deliver the child, lacerations of the upper vagina and, in suitable cases, lacerations of the cervix should also be repaired at once. It prolongs the use of the anæsthetic but a few moments to do the necessary suturing and, by sewing

up the tear, thereby closing the bleeding vessels, we save the patient from the loss of blood and restore the uterus to a condition by which convalescence is hastened. Most of the cases of so-called post-partum hæmorrhage are due to a lacerated cervix, and I believe the same rules should apply here as in other regions of the body. If the cervix is not repaired at the time of delivery, in the vast majority of instances this can be done before the patient leaves her bed. The edges of the tear can be freshened with the curette, and primary union is obtained in practically all cases. At this early period there is little or no thickening of the edges of the wound, and close apposition is easily made. Most of the tears can be sutured without the aid of a general anæsthetic.

After inspection of the outlet is made and all necessary repairs completed, the parts are cleansed with a 1:2000 solution of mercuric chloride, poured on from above and allowed to run down over the vulva. The washing is completed with cotton sponges wrung out of the same solution. In washing, the sponges are used with a downward stroke only, and each sponge thrown away at the completion of the stroke. The region of the anus is to be avoided until the last. The first dressing of the vulva should be of gauze or cotton wrung out of a 1:4000 solution of mercuric chloride. All soiled clothing should be removed with the draw-sheet, a clean gown supplied, and the patient put to bed on her back, with her head low. She should not be allowed to turn on her side for the first two days. As rest is essential after so trying an ordeal, everything conducive to quietness should be carried out: the baby removed from the mother's presence, the room darkened, and all visitors excluded. No others than the husband and the mother should be allowed to visit the patient while she is in bed. There should be no douches, vaginal or uterine, as there will be no cause for either if the delivery has been accomplished under aseptic precautions. Gentle massage of the uterus through the abdominal walls will facilitate its contraction and cause the expulsion of retained membranes, blood-clots or other débris and assist in that process so much to be desired, an early and normal involution of the uterus and adnexa. After the first dressing the vulvar dressings should be sterile cotton or gauze next to the vulva, with a salicylated strip of gauze covering this and attached in front and behind to the abdominal binder. They should be changed as often as they become soiled. Before a fresh dressing is applied the vulva must be cleansed by pouring a solution of mercuric chloride, 1:2000, over the vulva without separation of the labia. All cleansings should be made from above downward, and all washings in the same direction. The nurse should keep a complete chart, noting all the conditions and peculiarities of the patient, in order that the physician may know at the earliest moment should any retrogressive change take place. At each visit of the physician the height to which the uterus reaches above the symphysis is noted. Its sensitiveness and contractility are determined by abdominal palpation, care being taken to ascertain at the same time the condition of the adnexa, especially with a view to the early detection of any inflammation occurring. If there is considerable tenderness in the region of the womb, and the organ is found to be relaxed and flabby, the physician's hand

is applied to the abdomen, and massage with gentle strokes instituted and continued until the organ is found to contract and the soreness disappears. This takes but a few minutes and enables the doctor to ascertain the size and condition of the uterus and to apply the appropriate treatment at one and the same time. I find this massage the best treatment for suppressed flow and the safest way to cause the expulsion of retained membranes and detritus from the uterus. It is a routine procedure with me, and, as previously mentioned, it hastens involution. In the way of drugs to promote this, ergotin or a special preparation made from Spanish ergot, with the addition of strychnine and acetylsalicylic acid, is valuable. When the after-pains are too severe to be endured, acetylsalicylic acid or codeine, either alone or in combination, will be found to relieve the suffering. If the pains are due to retained blood-clots, gentle massage of the uterus will cause them to be expelled and ergot and strychnine, by their tonic effect on the uterine muscle, will prevent their re-forming.

The amount and condition of the lochia should be carefully noted at each visit, and, when any appreciable diminution is manifested, gentle massage should be applied over the uterus. Any marked rise of temperature after the second day ought to cause a suspicion of infection, and investigation should be instituted at once. When the temperature reaches 102°, the uterine lochia should be submitted to a bacterial examination. After the specimen is secured, the uterus should be examined with the sterile index finger and the tubes and appendages explored. If the uterine cavity is smooth, sterile water or saline douches should be given at once; but, if the uterus contains débris, this should be removed with the finger before such washing out. The curette should not be used, and mercuric chloride, phenol, or other antiseptics are contraindicated. When the infection has extended beyond the uterus, local treatment should be discontinued. In gonorrhœal endometritis active treatment is not required at the time, as the majority of these cases recover spontaneously, or the patient is left with a chronic endometritis and disease of the appendages, which can be treated much more advantageously at a later period. Measures which will keep up the strength of the patient, such as general tonics, are the most valuable, and alcohol and strychnine in large doses are the most reliable drugs for the purpose. High fever is to be combated with cold sponges or baths, rather than with antipyretic drugs. Saline solution per rectum, by the drop method, should be instituted early. Where the infection has extended beyond the uterus and parametritis or peritonitis exists, the icebag or coil should be applied over the uterus and appendages in the early stages. Later, moist or dry heat should be applied to the lower abdomen. Parametritic abscesses should be opened through the vagina as soon as the diagnosis is made with certainty. Pus-tubes and ovarian abscesses, if movable, should be removed by laparotomy. If they are adherent and readily accessible, vaginal puncture should be performed, and the abscess cavity packed with gauze. Antistreptococcic serum has been demonstrated to be of value in puerperal infection only as an agent to stimulate phagocytosis. It seems to have some value when given early as a prophylactic, but is not to be relied upon. Most operators agree that in this condition

hysterectomy is usually contraindicated. Ligation of the thrombosed vessels, distal to the thrombus, seems to be more expedient.

The condition of the bladder of the puerperant should be noted carefully, as retention of urine following labor is frequent. The patient should not be catheterized until all other efforts have failed to cause her to urinate. She should first have hot applications applied to the region of the bladder, and hot sterile water poured over the vulva and applied to it by means of wet cotton or gauze, and an enema should also be given. Pressure should be made over the bladder, and the patient should be raised to a sitting position on the bedpan. The sound of running water sometimes has the desired effect. The catheter should be passed as a last resort, but the bladder should be emptied every twelve hours. Incontinence of urine after labor is usually due to an overdistended bladder. Pressure-paralysis of the *sphincter vesicæ* occurs in rare instances, and it is slow to yield to treatment. Tonics, electricity and massage give the best results. Cystitis is quite common during the puerperium, due to careless introduction of the catheter. In mild cases the patient should drink large quantities of fluids, such as milk and the carbonated and lithiated waters. For irritability of the bladder the balsams, such as copaiba or sandalwood, should be given, in 3- to 5-drop doses, in capsules, four times a day, or, instead of these, 5-grain capsules of phenylsalicylate or hexamethylenamine, repeated every four hours. When the process fails to yield to this treatment, daily irrigations of the bladder with a 2 per cent. solution of boric acid, or a 1:30,000 solution of mercuric chloride, should be practised in connection with the administration of tonics and stimulants. The infection may extend up the ureter to the kidney and cause a pyelonephritis, and this should be treated in essentially the same way as cystitis, unless a perinephritic abscess occurs, when the pelvis of the kidney should be incised. Hæmaturia in the parturient is caused by the dilatation of the veins induced by pelvic congestion in the last months of pregnancy, in consequence of the pressure of the child's head, by the use of instruments, or by a vesicovaginal fistula. It usually disappears in a few days.

The parturient should be given a laxative at the end of twenty-four hours after labor. Castor-oil is the best, but, if it should be too objectionable to the patient, magnesium citrate or phenolphthalein may be substituted for it. The last mentioned has the advantages of being tasteless and not affecting the child. The diet should, in some measure, be suited to the condition of the individual case, its character depending somewhat on whether or not the patient has lost a large amount of blood. Ordinarily, a diet consisting of milk, broths, weak tea, cocoa and simple soups, with the addition of milk toast, crackers, buttered toast, dry toast, soft-boiled or poached eggs, and any breakfast food, if thoroughly cooked, is suitable for the first two days. After the bowels have been moved well, a full dietary may be allowed, with the exception of pork, veal, corned beef, cabbage, turnips, cucumbers, canned corn, canned beans, vinegar, strawberries and melons, and any article that is known to disagree with the patient. The idea that the parturient should be starved is obsolete; she should have plenty of good food.

The patient should by no means lie on her back the whole time. After

the first two days she should be allowed to turn from side to side and encouraged to lie on her face for short intervals. On the fourth or fifth day she may be permitted to get up to the commode, with the assistance of the nurse, and to sit up in bed for short periods. She should have a limited amount of exercise while she is in bed, such as that afforded by passive and resistant movements, supplemented by body massage. The breasts should be supported early by means of a broad, firm bandage passing over them and around the chest. If they become engorged, tender and painful, sterile absorbent cotton should be plentifully applied about them, and pressure exerted by tightening the bandage. If this treatment is instituted promptly, the circulation will be controlled and with it the flow of milk. If, with the above treatment of the breasts, the nipples are now cleansed, before and after nursing, with a saturated solution of boric acid, there will be little danger of mastitis developing. The baby should not be allowed to go to sleep at the breast. If this is the case, the nipples are apt to become macerated, with resulting erosions and fissures, which are not only painful, but constitute open avenues for the entrance of micro-organisms. The baby should never be allowed to nurse on a sore or fissured nipple; for this painful condition a nipple-shield should always be used. Weak and very anæmic mothers, and particularly those suffering from any form of tuberculosis, should not be allowed to nurse their infants. This should likewise be forbidden in epilepsy, syphilis, chorea, nephritis and malignant disease, and whenever a woman is rapidly losing weight from any cause whatever. Lactation should be discontinued in a state of approaching pregnancy and, as a rule, it should not be kept up beyond twelve months.

There is a tendency to put all women through the same routine as to the time of leaving their beds, getting them up on the ninth or tenth day. Doctors are fearful of censure from the patient and her friends if she is not allowed to get out of bed by that time, and I believe a great amount of necessary treatment is neglected for fear of this censure. Before being permitted to sit up the mother should be carefully examined, in order to ascertain the size and position of the uterus and the condition of the birth-canal. If there is a displacement of the uterus, the organ should be replaced bimanually, and a proper pessary fitted to keep it in place. In some cases it is better to treat the condition with glycerite of boroglycerin tampons for a time before the introduction of the latter. About the only excuse the pessary has for its existence is in the early treatment of the displaced uterus of the parturient. If used in this condition, before fixed changes of the supporting structures have taken place, a pessary will prove most satisfactory. Where there seems to be an atonic condition of the uterus, antiseptic, astringent douches, varying from cold to hot, according to whether the condition is acute or chronic, may be used to accelerate the process of involution. Glycerin tampons are helpful in this class of cases by depleting the parts. All unhealed surfaces, the so-called puerperal ulcers, should be touched with phenol, iodine or silver nitrate, as the case demands. Great care should be taken, even at this late stage, to guard against infection, and nothing but the technique of aseptic surgery should be practised at all examinations and treatments. Sterile rubber gloves should be worn when examinations are

made, and the parts prepared antiseptically. Infection need not be of the degree to cause puerperal fever in order to subject the patient to danger. We have seen how readily an infecting germ may reach the ovary. If the infection is but mild it may yet be sufficient to cause a hyperæmia of the organ, which may be followed by a subinvolution resulting in a fibrotic or cystic condition, with the causation of lessened function. This is naturally followed by a diminished ovarian secretion, inducing an unbalanced condition of the internal secretions which may result in hyperthyroidism, with such symptoms as palpitation of the heart, sleeplessness, rapid pulse, flushes, etc.

The mother should lie face down for two hours every day for the first two months. She should lift her child as little as possible, and not carry it in her arms during this time. Relaxed abdominal muscles allow a low abdominal tension, with the effect of enlarged and distended veins and organs engorged with stagnated blood, overcharged with carbonic acid and other waste products. The supplying of this vitiated blood to the general circulation causes languor, backache, restlessness, irritableness and a disposition to give way to trifles and to weep at every turn, evincing a lack of mental poise. In all cases of relaxed abdominal walls, with or without ptosis of the viscera, where massage and exercise have failed to effect restoration, some support, such as a Storm binder or Rose bandage or, what, in the author's opinion, is better, a long, straight-front corset of the kind suggested by Dr. Gallant, should be worn. There should be no compression of the waist to interfere with the action of the abdominal muscles. The pressure should be between the ilia and the pubes, and when it is thus applied there will be a lifting effect which serves to hold the viscera in position.

All who would practise obstetrics should be able to thoroughly appreciate the value of time as the great factor in success. Let nature have her way. Not until the uterus is restored to its normal position, and all lacerations and weakened parts incident to parturition have been repaired, can the parturient be considered free from medical care. In this age of automobiles and airships there is a tendency to haste, to rush along, to "hurry up" things, and the doctor, imbibed with the spirit of the age, is likely to hurry the progress of labor by applying instruments before nature has had sufficient time to complete her work. In obstetrics the passenger and the highway of travel have always been the same, and there is little likelihood of either's ever being changed. Experience teaches us that, as we become more civilized, cultured and refined as a people, the slower and more difficult does child-bearing become. The two factors of most vital importance in the lying-in room are cleanliness and patience. In conclusion, I would suggest that the most important elements in the treatment of the puerperant are strict asepsis, the restriction of internal examinations to the minimum; careful massage of the uterus, daily for the first two weeks; to assist involution, the making of all necessary repairs of the weakened and lacerated parts early, and the prompt restoration of the uterus, if displaced, to its normal position, keeping it in place by means of some support until it will retain its position. If these measures are carried out we shall hear less often

from the patient the complaint: "Doctor, I have not felt well since my baby was born."

DISCUSSION.

*Dr. Barnes* said it was hardly possible to emphasize too strongly the necessity for getting the post-partum patient off of her back. Constant lying in this position tends to cause backward displacement of the organs. The patient should be encouraged to lie upon her face or side, or even to occasionally assume the knee-chest position. This seemed to him to be the most important point in the paper, namely, the need of doing away with the liability to the sagging back of a heavy uterus, with more or less permanent ill effects.

*Dr. Shoup* said that one of his objects in writing the paper had been to sound a warning against the routine practice of getting these patients out of bed and discharging them at the end of ten days, without taking into consideration the special condition of the patient in each individual case. As a result of this treatment, not a few of the patients come back with pathological conditions which might have been avoided by the exercise of greater caution on the part of the physician.

# DELAYED MENOPAUSE: ITS DANGERS AND THERAPEUTIC INDICATIONS.

## Presenting a Table of the Approximate Age at which, in Women Free from Pelvic Diseases, Disorder or Displacement, the Menopause Should be Established.

By A. ERNEST GALLANT, M.D.,
NEW YORK.

THE cessation of menstruation in the wholly healthy woman should occur abruptly, at an age-ratio dependent on the age menstruation commenced: late, if begun early, and early if begun late. So few women who are free from symptoms and apparently healthy at the time of the menopause apply for examination that accurate data on which to base the real normal relation of the beginning and end of the menses are extremely difficult to secure. We have therefore worked out the following table of "Approximate Ages" *as a practical working schedule* upon which to estimate the probable date of the menopause, as the age limit beyond which no woman should be allowed to go on menstruating without a thorough examination:—

APPROXIMATE AGE OF MENOPAUSE.

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Menses | begun | at | 10th | year; | should | cease | between | 50—52d | years. |
| " | " | " | 11th | " | " | " | " | 48—50th | " |
| " | " | " | 12th | " | " | " | " | 46—48th | " |
| " | " | " | 13th | " | " | " | " | 44—46th | " |
| " | " | " | 14th | " | " | " | " | 42—44th | " |
| " | " | " | 15th | " | " | " | " | 40—42d | " |
| " | " | " | 16th | " | " | " | " | 38—40th | " |
| " | " | " | 17th | " | " | " | " | 36—38th | " |
| " | " | " | 18th | " | " | " | " | 34—36th | " |
| " | " | " | 19th | " | " | " | " | 32—34th | " |
| " | " | " | 20th | " | " | " | " | 30—32d | " |

These figures are intended to represent the age-limit in healthy women only, and vary widely from the averages collected by E. Kriegar, which include all classes of women, regardless of general or pelvic disease.

Among 3700 patients seen by the writer in the gynæcological departments of the Roosevelt Hospital, O. P. D., and the Northern Dispensary, there were 278 who had reached or passed the menopause, and, of these, 154 could recall their ages when menstruation began and ended. Of the latter number, in 73, or 48 per cent., the menopause had been delayed beyond the "approximate age," including

| | | |
|---|---|---|
| 3 cases of carcinoma uteri, an average of | 7.0 | years. |
| 17 cases of flexion, version or fixation, an average of | 6.5 | years. |
| 15 cases of prolapsed uterus, vagina and bladder, an average of | 6.2 | years. |
| 4 cases of late recurrence, an average of | 10.75 | years. |
| 39 cases, a total of 266 years, or an average of | 7.00 | years. |

Of the same 3700 women, there were 484 over 35 years of age, 150 having passed the "approximate age" by a total of 837 years, or an average of 5.6 years, who were subject to one or another form of atypical menstruation amply justifying them in seeking relief from the burden of delayed menopause.

The menopause is "delayed" whenever menstruation is continued after the "approximate age," and this is always associated with uterine flexion, version, fixation, neoplasm, tubal disease, or syphilis, etc.

The *danger signals* in delayed menopause are: (*a*) atypical hemorrhage; (*b*) discharge; (*c*) pain; signals which, if disregarded, lead to disaster and death. The first case cited was that of a woman 40 years old, with cancer of the uterus, too far advanced to permit of radical operation. The symptoms were greatly relieved by the local application of acetone, and she died one year after coming under observation. The application of this agent, in incurable cases, to the excavated cervix, or after scraping away the cauliflower mass, as suggested by Gellhorn, Dr. Gallant said, had the effect of controlling the bleeding, abating the offensive discharge, and obtunding the pain to a remarkable degree. It also inhibits the growth, even though the fatal issue of the disease cannot be prevented.

*The Dangers Incident to Delay.*—1. Delay on the part of the patient in consulting a physician. Many women, through ignorance, false modesty, fear of examination, fear of learning the truth, or a wish to hide their condition from others, postpone this until too late.

CASE 2.—Mrs. McC., 55 years. Carcinoma of the uterus and anterior vaginal wall. The cervix a cone-shaped shell, excavated by the degeneration of the growth. Has had hæmorrhage and discharge for a long time. Of this variety of incurable cases he has met with about one hundred; some, naturally, varying in that the vagina was filled with a cauliform growth, and the rectum, bladder and vulva more or less involved; but all hopeless so far as any real curative treatment was concerned.

2. Delay due to absence of urgent symptoms:—

CASE 3.—Mrs. C. R., 42 years. Malignant ovarian cystoma. Menopause two years delayed. For the past three months her abdomen has rapidly grown larger. Backache when lying; pain on the right and center of abdomen; weight diminished from 175 to 140 pounds. Firm tumor reaching nearly to the umbilicus, on the left; uterus small and pushed against the symphysis to the right. Operation. Prognosis unfavorable.

3. Delaying examination. Not infrequently the gravity of the situation has not been appreciated by the physician, who temporizes and permits a malignant growth to advance to a dangerous degree, thereby lessening the chances of a cure.

CASE 4.—Mrs. M. E. L., 68 years. Medullary carcinoma of the uterus. Abdominal hysterectomy. Menses did not cease until some time after her fiftieth year. Backache and flowing off and on, with discharge since September 25, 1909. Up to February, 1910,

no examination per vagina had been made by the physician attending her up to that time. Operation, February 23, 1910. What is the prognosis in a woman of 68 years? and how much more favorable, had the uterus been removed some months or years earlier?

4. Delay through failure to make a correct diagnosis, leading to minor operation, where radical extirpation was imperatively indicated:—

CASE 5.—Mrs. H., 42 years. Carcinoma of the body of the uterus. Vaginal removal of uterus and right (cystic) ovary. Menopause delayed four years. On account of excessive, irregular flow, her physician, two months ago, curetted the uterus and repaired a lacerated cervix. Six weeks later the flow recurred and has continued, off and on, for the past six weeks. Bachache, not relieved by a pessary; has lost flesh and strength and usual activity. While this patient is now in good health, how much better and safer it would have been had she been examined at the approximate age and the enlarged, retroverted uterus removed.

5. Delay due to refusal of the patient to follow advice:—

CASE 6.—Mrs. M. B. Operation postponed thirteen years. She died something over a year after abdominal hysterectomy, having suffered all the tortures of malignant disease and vesicovaginal fistula. The floor of the bladder was infiltrated and it was accidentally perforated during the operation; attempted closure failed.

6. Delay due to the delusion that atrophy of a fibroid uterus will occur after the menopause:—

CASE 7.—Miss B. E. S., 45 years. Large fibroid uterus; excessive debility and anæmia from hæmorrhage. Abdominal hysterectomy. If the operation had been done earlier she would have been saved six months' or more loss of time, to say nothing of much mental and physical suffering.

7. Delaying operation for fibroma results in severe oligocythæmia and oligochromæmia, which seriously handicap the patient for subsequent hysterectomy, even in those who have not attained the approximate age.

CASE 8.—Mrs. R., 33 years. For four months had been losing an excessive amount of blood, notwithstanding the administration of hæmostatic drugs to the limit of ergotism. The fibroid uterus was removed by abdominovaginal hysterectomy, and she succumbed two days later; a victim to her own willful delay.

8. Delaying the removal of fibroma results in malignant degeneration of the growth:—

CASE 9.—Mrs. C., 55 years. Abdomen distended by a fluctuating tumor especially prominent on the right side, and which projects downward, filling the whole pelvic cavity. The temperature (101° F.) obscured the diagnosis and led him to evacuate through the vagina. More than a quart of débris consisting of disintegrated fibroid, clots and fluid escaped, followed by collapse of the tumor. The small uterus lay toward the left. In spite of rubber-tube and gauze drainage the tumor rapidly enlarged, and eight weeks later the mass was removed by cœliotomy. Some of the gelatinous material must, however, have entered the peritoneal cavity, which again refilled, and she died in less than a month. Pathologists' report—sarcoma.

In cases of cervical or uterine polypi, which are not infrequently met with in delayed menopause, hysterectomy would scarcely be indicated, though at times polypi appear to be the forebears of malignant disease. When examining women one must not mistake the bleeding coming from a urethral caruncle, anal fissure, or internal hemorrhoids, which possibly may suggest neoplasm.

9. Delayed menopause is most frequently due to or associated with *uterine obstruction.* At the meeting of the society last year, Dr. Gallant, by an analysis of 185 cases, had endeavored to show the importance of chronic obstruction to the uterine outflow, menstrual and intermenstrual, and the manifold serious consequences which might result from this, and he now reiterated his positive conviction that every menstruating woman, at whatever age, can be, is entitled to be, and ought to be promptly treated for all menstrual irregularities, pelvic pains, backache, headache, etc., not only for the relief of these distressing symptoms, but as a means of "heading off" the more serious danger, the development of benign or malignant neoplasms.

*Prophylaxis.*—At the approximate age the woman has reached the limit of fecundity; therefore the *prophylactic removal* of a useless, and probably dangerous, tumor-breeding organ is wholly justifiable, and the one sure method of putting an end to all the dangers.

Prophylactic hysterectomy for hereditary cancer of the uterus:—

CASE 10.—Mrs. K. K., 38 years; five living children. Has suffered from very excessive flow for twelve years. The large, heavy uterus was held firmly in the hollow of the sacrum, and could not be replaced bimanually. Owing to the fact that her mother and grandmother had both died of cancer, one at 65 and the other at 45, it seemed to him that to allow this uterus to remain would be to jeopardize, unnecessarily and unjustifiably a life so valuable and necessary to her five living children. It was therefore removed by the vaginal route, on May 17, 1905, and the patient is now healthy and very happy because the danger has been averted.

Having related a case in which prophylactic hysterectomy was done for external prolapse of the uterus and bladder, and one in which this was done for excessive hemorrhage due to syphilis, Dr. Gallant gave a summary of the various points treated of in the paper, concluding with the following: The large number of incurable cases met with of carcinoma uteri, degenerated fibroids, and malignant ovarian and broad ligament cystoma, which sometimes develop as early as the twenty-fourth year, shows the necessity of instructing mothers to warn their daughters of the dangers of delay whenever they suffer from dysmenorrhœa, menorrhagia, metrorrhagia, leucorrhœa, abdominal tumors, etc., especially after they have passed the approximate age.

# THE TREATMENT OF "PARASYPHILIS" OF THE NERVOUS SYSTEM IN THE LIGHT OF RECENT RESEARCH: PARESIS AND TABES DORSALIS.

By TOM A. WILLIAMS, M.B., C.M. Edin.,

Memb. Corresp. Soc. de Neurol. de Paris; Memb. Corresp. Soc. de Psychol. de Paris; Memb. Assoc. de la Soc. de Méd. Ment. Clin.; Neurologist to the Epiphany Dispensary,

WASHINGTON, D. C.

*Status of the Question.*—Incurability by specifics has been regarded as one of the main characteristics of the quaternary manifestations of syphilis, paresis, tabes dorsalis, leukoplakia, etc. This was not only the dictum of alienists, to whom patients went after disintegration of the nervous system, but syphilographers of the eminence of Fournier[1] acquiesced in this verdict of pessimism. So the matter rested, with an occasional dissentient voice, until the pathological studies of Nageotte[2] clearly showed the directly syphilitic nature of taboparesis, and stimulated, especially in France, trials of mercurial medication in cases of tabes dorsalis. In spite of occasional successes, it was to only a few that the valency of this therapeusis appealed; until, as it seems only yesterday, the Bordet-Gengou[3] principle was so brilliantly applied in the hands of Wassermann,[4] and showed unequivocally the pathogeny of the once-called metasyphilis. The data of Wassermann, Plaut[5] and others further stimulated inquiry into the relationship between complement deviation and antisyphilitic medication in so many cases of tabes and paresis and into its success in a number of others.

Up to the present, there is much difference of opinion about the influence of mercury upon the Wassermann reaction. A factor in the settlement of this would seem to be the absence of the reaction which sometimes does not take place in the fulminating cases, though it occurs in practically every paretic. Müller,[6] of Vienna, Eichelberg,[7] and others believe that as an index to treatment the reaction is of little value, and that its absence should not make us cease intermittent medication. There is, however, a tendency to look upon the test as a guide to continuance of treatment; which it cannot pretend to be, judging from the data so far presented. In France, the test is not even regarded as a specific one,[8] although recently Flashman and Bullock[9] have made a strong plea that it be so regarded.

It is curious that latent syphilis sometimes lights up apparently as a direct result of mercury. The only valid explanations so far adduced seem to be, on the one hand, the stimulation of the spirochæta by the inimical substance, mercury, and, on the other hand, perhaps, the interference with antibody production by the same agent in certain individuals. Some pharmacologists, on the contrary, believe that the real manner of action both of mercury and of the iodides is their effect as stimuli of the defense-mechanism of the body. As regards mercury at least, this explanation would appear to be contradicted by Metchnikoff

and Roux's[10] experiments on apes, whereby they prevented infection by calomel ointment applied within twenty-four hours of the access of the virus to the mucous membrane. The repetition of this upon his own person by Mazenove[11] showed its applicability to human beings, and that this is not an exceptional case is proved by the results of the prophylaxis now adopted in the American navy,[12] namely, that every man on his return from shore-leave is given the opportunity of a toilet of which mercurial inunction of the glans forms a part. When we realize the powerful germicidal effect of mercurial preparations, it would require stronger evidence than we have at present to warrant the conclusion that the internal secretions play a material part in what appears to be a destruction of the spirochæta before it has reached the submucous tissue.

These considerations have an important bearing upon the meaning of mercurial medications; for it must be remembered that our forebears numbered mercury among the deobstruents, by which term they described substances which facilitate the disappearance of hyperplasia of all kinds. The most powerful agents of this class are, of course, the iodides, and it is to this function of these latter that we now attribute their usefulness in gummatous affections. It is not believed that their germicidal or antitoxic power is considerable as regards the spirochætæ, and their use in syphilis, even in the tertiary stage, is relegated on the continent of Europe to a strictly secondary place. In this notion the influence of Jonathan Hutchinson has prevented acquiescence on the part of English-speaking physicians; but latterly, even here, mercury is becoming more and more recognized as the paramount drug, even against tertiary lesions. This being the case, is mercury not applicable to the late tertiary manifestations of syphilis? Here I can speak only of that part of the body to which in recent years my therapeutics has been confined, the nervous system. As it is facts which count when a classical doctrine is assailed, I cannot do better than present to you the summary of a few cases of quaternary syphilis of the nervous system successfully treated by mercury. I shall present only seven, and, lest you should suppose that I am alone in this opinion, three of these cases will be selected from the experience of Charles Dana,[13] the eminent neurologist of New York, and another from the work of Vincent,[14] a pupil of Babinski and Majestie, whose work upon tabes has so clarified our conceptions of the pathogenesis and treatment of that disease.[15]

CASE 1.[16]—Man, aged 40, referred May, 1908, by Dr. Lewis L. Taylor for a severe nervous breakdown following "indigestion" for five years.

*Previous History.*—Moderate smoker and rarely took alcohol; had given up coffee. Eats well. Single from choice. No sexual excesses. Infected twenty years before. Since nine years has felt useless and depressed, almost wanting to die. Attacks of desperate desire to flee. Since two years, dyspnœic and sinking feelings, occurring suddenly without external cause, light feelings in the chest, thumpings in the heart. Nervous chills with tremor, crying spells, voice tremulous and uncertain. For a year and a half had given up his bank, and taken up out-of-doors soliciting; during which time he had gained ten pounds.

*Examination.*—Foul breath, thickly furred tongue; circulation, respiration and urinary functions normal.

*Nervous System.*—Deep reflexes all exaggerated; the triceps, patellar, Achilles

and deltoid unequal on the two sides. The cutaneous reflexes, including the plantar, diminished. Pupils react normally.

*Motility* deficient in the left forehead; trembling of left cheek, of tongue and right fingers. Adduction of right thigh imperfect. The left heel left the floor while he sat up from recumbency. *Sensibility* unimpaired.

*Psychic Functions.*—Memory not impaired; perception clear; calculation slow and imperfect.

*Treatment.*—He was given a mercurial course during seven weeks, when he went to the mountains with all the symptoms vastly improved. He was then able to do office work without fatigue or irritability. In October a second course was given, and he could now stand the pain of mercurial cream injections once a week. He has since then remained well. I should add that a very careful régime and a restriction of the proteids in the food were instituted.

CASE 2.[17]—Man, aged 54, seen with Drs. Prentiss and Main on account of a "neurasthenic state," present six months, which rest, change and a sea voyage had benefited only slightly and temporarily. His complaints were insomnia, irritability and a state of suffering and incapacity; had been subject to hardly noticeable depressions and exaltations every few years. He has no children.

*Examination.*—In spite of cold weather, an abundant sudorrhœa of both axillæ and the internal border of the left arm; less abundant on the left leg.

*Motility* strong; no tremor of tongue, face or eyes; but the right platysma trembles, and there is a rhythmical tremor of the arm.

*Sensibility.*—A zone corresponding to fifth lumbar and first sacral roots insensible to vibrations.

*Reflexes* uneven, that of the right knee being diminished and the abdominal and right plantar almost absent. Pupils irregular, and the light reflex imperfectly maintained. The speech is slightly drawling, and a word or letter occasionally stuttered over.

*Psychic Functions.*—Memory slightly below normal; calculation slightly imperfect. During the first examination his insight seemed impaired, as he was quite indifferent. He declares that his lack of interest ensues upon peculiar abdominal feelings, like the sensation after a debauch, followed by a sinking feeling and misery.

*Treatment.*—He was at once given mercurial injections, and a few days later the examination was continued, and showed him to be incapable of detecting the glaring impossibilities depicted in some drawings I use for the purpose.[18] His steady improvement was interrupted only once by an error of diet. After five months of hard work on a farm he began to feel nervous again; but another course of mercury arrested the symptoms. Six months later some unusually hard work caused another relapse; but I believe that a short rest will restore him completely.

CASE 3.[13]—Man, aged 40. Was infected before he was twenty. Had ideas of power and self-reproach, later a distinct melancholia. The pupils were unequal. Left knee-jerk was lively; the right weak. He had tremor of hands, but none of the face. He suffered from insomnia; no headaches, no cranial nerve palsies except those of the eyes. In six months he was practically well.

CASE 4.[13]—Man, aged 37. Infected twelve years before. The pains and paræsthesias extended down the back of the neck and shoulders. He was depressed, his memory poor, his speech syllabic. He had no tremor, and the pupils and knee-jerks were normal. He had at times some brief illusions, but no hallucinations. He was sent to a sanitarium for several months. Since that time, a period of four years, he has continued well.

CASE 5.[13]—Man, aged 46. He had syphilis at twenty-three, and received treatment. At thirty-four he had some mental depression and rheumatic pains. He was relieved by hypodermatic treatment with mercurials. He married at thirty-seven and had a healthy child. At forty-six he had nervous attacks consisting of agitation and trembling, and he had suffered from dyspepsia. He also had had an "anxious depres-

sion," or mild form of hypochondriacal melancholia, which did not keep him from work. No objective symptoms. He gradually recovered, but a year later complained of entire loss of sexual power, failure of memory, difficulty in concentration at work, and dyspeptic symptoms. At the end of a year he was well except for sexual weakness. No symptoms of tabes. From the age of thirty-four to forty-six he took mercury by subcutaneous injection; at first every two weeks for two years. These injections acted as a tonic, the effect lasting for two weeks. Later he took the treatment at much longer intervals.[16]

CASE 6.—That of a physician who was seen three years ago by an eminent ophthalmologist on account of diplopia, and unfortunately our distinguished colleague did not ascertain the cause, but merely prescribed glasses to remedy its effect. Some months later a severe nervous breakdown and peculiar conduct with dementia led to a unanimous diagnosis of paresis by Drs. Starr, Dercum and Brush. I had occasion to see him while visiting another patient in the sanitarium where he was, and strongly urged upon the director the trial of mercury, although the patient had been confined there for nearly a year, and was quite defective. The result was that before six months the active manifestations ceased, and the patient became quiet and able to perform a considerable amount of ordinary work. Owing, however, to the long-continued destruction of cerebral tissue, his intelligence lacked its former capacity, and he was somewhat childish in his judgments one year after the commencement of treatment. Now, this case is not adduced as an example to follow, but merely as an instance of the influence of mercury over parasyphilis of the brain, even though considerable dementia is present. We should aim at early diagnosis, which in my first two cases and those of Dana led to a practically complete restoration to health.

The *technique* is of the greatest importance, if injections are not to be discredited as a procedure. A full consideration of this subject may be found in the monograph of Levy-Bing (Paris, 1909). I shall only indicate my own method. For both soluble and insoluble preparations, I find that a needle of platinum-iridium (about 2 c.c. to 3 c.c.) is sufficient, and I use the Luer all-glass syringe. In both cases the injection must be made deep into a muscle, preferably the gluteus maximus, although some therapeutists prefer the deltoid. The crural muscles, and in fact all those of the limbs, seem to be intolerant of the injections. The superior and outer third of the buttock is the place where one is most certain to avoid large blood-vessels and the sciatic nerve. Levy-Bing fixes the place of election by dropping a perpendicular to bisect a line joining the anterior superior spine of the ilium with the summit of the intergluteal fold. Within 3 c.c. of this center he places every injection, dividing the imaginary circle into quadrants, into which he injects by turn. Another rule is to place all the injections within a transverse zone one inch above the trochanter and one inch below the iliac crest. The injections are given in alternate buttocks, into the inner, middle and lateral segments of each horizontal zone in turn until twelve injections have been given.

*Frequency and Dosage of the Injections.*—Insoluble preparations are absorbed slowly, so that large quantities can be given at long intervals. One grain once a week is an average dose, which in many instances may have to be exceeded, either by increasing the quantity or shortening the interval. This is the method used by Colonel Lambson with great success in the British army. A good deal of pain occurs for a day or two after the injection, so that the method is not always applicable in practice. An emulsion of mercury in a

combination of hydrous wool-fat or palmitine has proved the least painful, but calomel has a more powerful therapeutic effect. Of the soluble preparations, corrosive mercuric chloride is the easiest to prepare, and in my hands has not given rise to any considerable pain; but the French writers prefer mercuric benzoate or iodide. The dose of either of these is about 2 cg., upward, and of the bichloride, about half this. I have had no experience with the cacodylates; for the accidents which have been reported after their use have made me unwilling to try them. Whichever preparation is selected, it must be injected deeply into muscular tissue, in a solution of about ½ per cent. I need not insist upon the precautions of asepsis of hands, instruments and patient. Some twenty to thirty injections should be given at the beginning of the treatment; then two weeks of interval should be allowed, followed by another series of twenty or more injections. Finally a series of six weekly insoluble injections may be given four times a year.

Jonathan Hutchinson is an advocate of the continuous administration of mercury, as against the intermittent method advocated more especially by Fournier. As we do not know the rationale of mercurial medication, only experience can determine which is the preferable plan; but the quantitative estimation of therapeutic experience is notoriously uncertain and takes a long time to effect a decision. Accordingly, an analogy must be sought until further data can be accumulated. Perhaps the best is the action of quinine against the plasmodium malariæ, and here experience has shown that the drug should be given in such a way that the content of the blood should be highest during the efflorescence of the parasite. Now, both the trophonema and the spirochæta are animal organisms, and many pathologists believe that spirochætæ undergo a cycle of development. Close clinical study may reveal symptomatic variations attendant upon different phases of the spirochæta's development, in correspondence perhaps with metabolic oscillations of its host, or perhaps independently of these. By trial we may find during which of these phases mercury produces its maximum effect against the parasite, and, if we succeed in finding this, much mercurialization will be saved our patients in the future, in the same way as cinchonism is at the present time reduced to a minimum while treating malaria. At present, both the intermittent and continuous methods aim at prolonged saturation with mercury, so that during this medication a spirochæta will always meet with an antagonist, whenever its susceptible phase may occur; but, to effect this, it is necessary to add greatly to the demand upon the renal function, and to disturb metabolism with mercury, for weeks at a time.

If experiments show these considerations to have a basis in fact, there will be only one way to exhibit mercury, and that will be directly into the circulation by injection through a vein. Even now there are many advocates of this as the method of election in ordinary cases, and all who have tried it are agreed as to its superiority in the fulminating case. Thus, Froguet,[19] in Abadie's clinic, has given eight thousand such injections in cases of tertiary and quaternary ocular syphilis, such as incipient optic atrophy and paresis of the ocular muscles. A striking case is that reported by Vincent and quoted by the writer in his article on the "Pathological Prodromes of Taboparesis:"[20]

CASE 7.—A man, aged 24, had syphilis, without secondary symptoms, in 1904. He commenced using gray oil from the time he saw the chancre, treating himself, but soon ceased on account of the pain, and substituted a daily dose of 10 centigrammes of mercuric iodide. This he continued for three years. Then, believing himself cured, he married. Twenty-seven months after the chancre, however, headache began, and this lasted almost continuously for eight months. Though worse at night, it was thought in turn to be influenzal, neurasthenic and neuralgic. On examination, no signs of organic nervous disease were discovered, but punctures showed an enormous lymphocytosis, such as appears in the most active cases of general paralysis. Indeed, the diagnosis could have been made with the naked eye, the liquid showing a peculiar opalescence characteristic of an abundance of cells. In addition to the usual cells, there were some of the polynuclear and eosinophile varieties and also some plasma cells. He was at once treated by intravenous injections of mercuric cyanide every other day, to the number of thirty in all. The headache quickly disappeared; but he was then given six injections of gray oil and four series of six injections each of emulsified calomel. He might have been considered as cured but for the appearance of a pharyngeal gumma, six months later, and for the persistence of the intense meningitis shown by the lymphocytosis.

Wernigk,[21] of Los Angeles, treats all syphilitics by the method mentioned.

*The Prognosis.*[22]—Two factors must be estimated in this: First, arrest of the disease. If the constitutional state is not grossly impaired, this can generally be accomplished. Second, restoration of functional capacity. The cause of tabes is a luetic leptomeningitis, as is indicated by the increased cellular content of the cerebrospinal fluid. This implicates the spinal roots, and, once the fibers of these are destroyed, regeneration of those within the spinal cord can never occur. Their function is lost forever, although it may be compensated for in part by those fibers which remain. Hence the supreme importance of diagnosing[23] the prodromes of taboparesis. Long before there is locomotor ataxia, loss of the knee-jerk, and pupillary rigidity the disease should be suspected from the *modifications of the sensibility,* such as the twinges of pain so often miscalled rheumatism. Still more often mistaken are the paræsthesiæ, itching, burning, tingling, dull, numb feeling, etc. Irritable bladder is frequently treated for months by urologists as cystitis, when its real cause is inflammation of the spinal roots, the prodrome of tabes. Genital irregularities are another source of mistakes. It is unfortunate that the neurologist is so seldom given the chance to see a patient whose disease declares itself in any of the above ways, but the gastric crises should be so well known that there can be no excuse for the frequency with which gastroenterostomy is performed through an error of diagnosis. Other pretabetic manifestations often overlooked are nervous diarrhœa, tenesmus, laryngeal cough, and chronic aortitis; while paralytic strabismus and other palsies, although common enough, are less unlikely to receive neurological advice, and hence give the patient an earlier chance of the diagnosis which may lead to the arrest of his disease before the disablement of some organ.

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## DISCUSSION.

*Dr. Fisher* said that too much emphasis could not be laid upon the desirability of an early and correct diagnosis. He had several times discussed with Dr. Dana the cases of the latter which had been cited by Dr. Williams. In most of them there is some ground for a difference of opinion as to the correctness of the diagnosis, as the cases were in such an early stage of the disease. The most difficult point is to make a differential diagnosis between general paresis and cerebral syphilis. Both give rise to a similar set of symptoms. Cerebral syphilis, however, is responsive to treatment. Many of the cases could and would go on to general paresis unless they received proper treatment, and then we are not apt to get the good results from treatment which could have been obtained in the early stages, so far as a cure is concerned. Can we relieve the symptoms in well-advanced cases? He believed that we can, in spite of the opinion of some clinicians that the iodides do no good in these cases, and that they may even cause, or hasten, optic atrophy. He was convinced that their use is followed by beneficial effects in many cases. The tonic effects of mercurial injections were well illustrated in an advanced case of tabes which came under his observation. The gastric crises recurred at least once a month and sometimes two or three times a month, or even more frequently, and morphine had to be given to the point of causing a habit. Mercurial injections in this case did great good. In general it can be said that the results in tabes and paresis depend largely upon the treatment which the patient received when the disease was in its early stages.

*Dr. Williams* said that the essential importance of the general hygienic management of patients who are taking mercury was not sufficiently appreciated. A patient whom he was treating with mercury began to do badly, although he appeared to be carrying out the treatment faithfully. An investigation showed that he had not been following the directions with regard to diet; he had been eating too much meat at night. When the diet was properly regulated all went well again. He was gratified that Dr. Fisher had corroborated his views as to the value of early diagnosis in these cases. Only with this can the best results be obtained.

# ON MORBUS BASEDOWI.*

By CARL BECK, M.D.,
NEW YORK.

As long as it is assumed that morbus Basedowi is produced by faulty chemical activity on the part of the thyroid gland, it is natural that the therapy of the so-called Basedow symptoms should be directed against the thyroid sphere. The most effective procedure naturally consists in thyroidectomy (notably without injuring the parathyroid bodies). The mortality of this operation still being a considerable one, however, a compromise is advisable. This is best reached by exsecting the largest lobe only, and treating the smaller one later on by the application of the Roentgen rays. Thus the danger of the operation is greatly lessened, and the size of the remaining lobe may be diminished at will by irradiation. The fact that the Roentgen rays influence the walls of the blood-vessels by producing an inflammatory reaction in them, so that a shrinking process is induced, was father to the thought of irradiation in morbus Basedowi. According to the statistics in the German translation of Dr. Beck's textbook on "Surgical Diseases of the Chest," most patients affected with Basedow goiters of moderate size improved considerably under simple Roentgen treatment. Modus operandi: Roentgen treatment is given through the diaphragm. with the patient in the sitting posture, for five minutes. In large goiters the anterior surface is irradiated for three minutes, while lateral irradiation of the goiter is kept up for one minute on each side. Small goiters are exposed in front only. When the patient shows much uneasiness during the séance, on account of tachycardia, frequent intermissions are made. As a whole, an exposure is advisable every two days until a slight reaction of the skin points to beginning dermatitis. Then the exposures are stopped for about a week, to be resumed again at the same intervals until there is a repeated reaction. At this period improvement also becomes manifest. If there are no severe reactive symptoms, the exposures may now be given once a week for a greater length of time. In the meanwhile the Roncegno iron-arsenic water is administered in doses of a tablespoonful, three times a day. Cases of short standing generally improve quickly. The tormenting nervous symptoms, especially, disappear first, and the dyspnœa produced by the tachycardia decreases after a few séances. The exophthalmos disappears only slowly, and in some cases a distinct trace of it is left long after the disease is virtually to be regarded as cured. It stands to reason that, with the disappearance of the main symptoms, general euphoria becomes more and more marked.

* Abstract.

# SURGERY OF THE OBESE.

By ROBERT T. MORRIS, M.D.,
Professor of Surgery in the New York Post-Graduate Medical School and Hospital,
NEW YORK.

In dealing with very fleshy patients we have to take into account certain conditions in physiology peculiar to the individuals of this class, and it is necessary to give consideration to a few very important mechanical points. In making incisions through the adipose tissue it is essential to make very clean cuts, in order to cause as few fatty tabs and irregularities as possible, because such tissue is poorly supplied with blood. In hæmostasis it is well to avoid the use of artery forceps if we can, because artery forceps crush a certain amount of tissue which must be disposed of by the lymphatics, and the lymphatics of the adipose tissue are neither abundant nor active, as compared with those of some other structures. If, instead of using artery forceps, we slip a ligature under each vessel by means of a needle, it lessens the amount of ragged tissue. When we have to tie a ligature through a mass of fat, the amount of fat included must be as small as will suffice, and the ligature must be drawn with an unusual degree of snugness, because the oil within the grasp of the ligature responds to the ordinary principle in hydrostatics, and slowly moves out of the way of the pressure. This may leave the ligature loose in an hour after it has been tied snugly enough to control hæmorrhage at the time of operation. Where we have to ligate a series of vessels lying near together, as in the fatty mesentery, in bowel work upon an obese patient, it is often best to run a continuous suture along the face of the cut mesentery with its opened vessels, and at each turn about the vessel take a half hitch with the suture. This step in technique saves considerable time, avoids much injury to fatty tissues, and disposes of the danger of loosening of the parts within the grasp of the suture material in an hour subsequent to operation.

During the entire time when we are at work with an obese patient, free oil is escaping, and the natural tendency would be to wipe this out along with blood and serum; but the adipose tissue must not be brushed, for gauze or sponge injures its texture and liberates still more oil. We have to depend upon the principle of filling the wound with salt solution and allowing the free oil to float to the surface, and then to float away in an excess of salt solution. This is a very important step in procedure. In suturing the muscles of the obese we often observe the fatty degeneration of muscle structure, and suturing through such muscle liberates free fat. Consequently, we must make it a rule to suture muscle-sheaths of fibrous tissue as far as possible without carrying sutures into the muscle itself, if it can be avoided. In fact, we try to make incisions in the obese in such a way as to avoid muscle-belly suturing later.

It is in final closure of the wound that one's nicest mechanical sense is brought into play, and here we fortunately have a resource of remarkable

importance, but one which is commonly overlooked. This is the resource of atmospheric pressure. Most of us, when boys, used as a toy the wet leather sucking-disk fastened to a cord. This we would press over stones and then lift them from the ground. When our teachers explained to us that our ability to lift these stones with the leather disk was due to atmospheric pressure keeping the leather in contact with the stone, it gave an object lesson which we can remember to advantage in later years as surgeons dealing with fatty wound walls. No sutures are to enter the fat. The muscles having been sutured beneath the adipose layer, the skin is next sutured, and before making the final knot the adipose wound margins are pressed firmly together between the hands, in order to express any air or fluid. The suture then being completed, atmospheric pressure holds the fatty walls together just as snugly as the wet leather disk of the boy is held to the stone, and we get a very much smoother line of union than was customary when the special suturing for these tissues was employed. If any extra supports are required for the walls of the wound, we can place two squares of adhesive plaster at a safe distance from the margins of the wound line, and then lace these together through eyelet-holes made with a punch and eye-carrier. The catgut or silk lacing which actually touches the eyelets will not be aseptic, but with a little care the part lying next the wound may be kept safe. In order to allow the escape of any culture medium which may collect in the wound during the first twenty-four hours, I poke a tiny wick of gauze surrounded by gutta percha tissue into the wound at any convenient point, and this is removed on the following day. As a matter of fact, the extra support made of adhesive plaster need not be put on until two or three days after the operation, or at about the time when catgut sutures would begin to lose their hold. The ordinary snug bandage or binder will support the walls of the wound well enough until that time. In former years I thought it necessary to use various supports, such as silkworm gut or silver wire, carried deeply into the adipose tissue and fastened to lead plates upon the abdominal wall, but a certain amount of liquid fat must escape along the line of any such supporting suture, and this will either burrow or make its way to the surface, inviting the entrance of bacteria and interfering with the nice apposition which we get by depending upon atmospheric pressure alone.

# THE PRESENT STATUS OF DRUG ADDICTION IN THE UNITED STATES.

By LYMAN F. KEBLER, M.S., M.D.,

Chief of the Drug Division, Bureau of Chemistry, United States Department of Agriculture,

WASHINGTON, D. C.

THE thoughtful and foremost medical men have been and are cautioning against the free use of morphine and opium, particularly in recurring pain. The amount they are using is decreasing yearly. Notwithstanding this fact, and the fact that legislation, federal, state and territorial, adverse to the indiscriminate use and sale of opium and morphine, their derivatives and preparations, has been enacted during the past few decades, the amount of opium per capita imported and consumed in the United States has doubled during the last forty years. Not only has there been this increase in the use of opium, its preparations and derivatives, but large quantities of other habit-forming drugs have been used initially, introduced chiefly for medicinal purposes. For example, cocaine[1] (cocaine hydrochloride) has been employed for about twenty-five years, and the amount consumed at present per annum is estimated at approximately 150,000 ounces, an amount ten times as great as actually needed. In addition to this, it is well known that large quantities of acetanilide, antipyrine, acetphenetidin and diacetylmorphine, and smaller quantities of hydrated chloral, codeine, para-aminobenzoyldiethylaminoethanol, etc., are used. The amount of opium imported per annum during the past twenty years is slightly less than 500,000 pounds. The average decrease per annum during the past ten years is about 20,000 pounds. The present deterring factors are antinarcotic legislation and publicity. From a comparison of the amount imported here with that in countries having efficient restrictive legislation, like Austria-Hungary, Germany, Holland, Italy and Spain, it is clearly evident that from 80 to 90 per cent. of the opium imported is used improperly. Based upon the statistics of these countries, and granting that there are at present 90,000,000 people in the United States, 50,000 pounds of opium would be ample for all legitimate purposes, but let us be liberal and place the amount so employed at 100,000 pounds. This would still leave over 350,000 pounds for paving the way for drug habituation. It is variously estimated by those who are conversant with the situation that the number of drug habitués in the United States varies from 1,000,000 to 4,000,000. The latter estimate is probably too high. The number is, however, so large, and the evil has made itself so distinctly felt in business, society, and even in the

[1] The words "cocaine," "codeine," and "morphine," as used in this article, refer to the salts of the respective alkaloids.

home, that observing, thoughtful men and women in various walks of life have been and are exerting their influence to bring about more stringent State and federal laws. Most of the States have enacted laws forbidding the indiscriminate sale of cocaine and cocaine-bearing products, and to a certain extent this also holds true for morphine and preparations containing it. Still, in many instances, there are some features which do not render such laws as effective as they might be. Many States are enforcing local laws regulating the sale of morphine, cocaine, etc., within their jurisdictions, but they are unable to control the introduction of these habit-forming drugs from localities outside of the State, and for this reason the officials find it very difficult to make material headway. Manufacturers, importers and wholesalers, until recent years, have been supplying these agents to all comers, but recent activity shows that they are anxious to see the illegal use of such habit-forming drugs suppressed, notwithstanding the financial loss which they may encounter. It is a well-known fact that many wholesalers refuse to sell undue amounts of cocaine to retailers, and from this it can readily be seen that there is a decided movement on foot toward suppressing drug addiction, not only on the part of the public, but also of manufacturers and dealers in these commodities. It is well known that there are many factors at work tending to drug enslavement, among them being the host of soothing syrups, medicated soft drinks containing cocaine, asthma remedies, catarrh remedies, consumption remedies, cough and cold remedies, and the more notorious so-called "drug addiction cures." It is often stated that medical men are frequently the chief factors in causing drug addiction.

In this paper I shall consider the following points: 1. What are the predisposing and exciting causes of such an army of unfortunates? 2. Is the number increasing or decreasing? 3. What occupations furnish the greatest number of addicts? 4. What measures should be taken to minimize or eradicate the evil? 5. Is there any known substance or mixture of substances which can of itself remove the craving of habitués for the following drugs: Cocaine, hydrated chloral, cannabis indica, opium, morphine, etc.? In order to obtain information on these subjects, letters were addressed to practising physicians, sanitariums treating drug addiction under direct supervision and sanitariums treating it both under direct supervision and in absentia only, throughout the United States. The data thus secured, with observations, follow:—

## RÉSUMÉ OF REPLIES BY PHYSICIANS.

*Question 1.*—In your experience what are the most common causes which tend to bring about addiction in case of each of the drugs named below: Opium, morphine, diacetylmorphine, cocaine, hydrated chloral, cannabis indica, and other habit-forming drugs?

| | Opium | Morphine | Diacetyl-morphine | Cocaine | Chloral | Cannabis Indica | Other Drugs |
|---|---|---|---|---|---|---|---|
| 1. First used remedially: | | | | | | | |
| (*a*) Careless prescribing or using by physicians | 25 | 35 | 23 | 21 | 21 | 19 | 19 |
| (*b*) Careless prescribing by drug clerks, dentists, osteopaths and others | 7 | 9 | 7 | 7 | 6 | 5 | 6 |
| (*c*) Physicians' prescriptions | 21 | 25 | 15 | 11 | 16 | 12 | 11 |
| (*d*) Self-medication | 13 | 12 | 6 | 13 | 10 | 7 | 10 |
| (*e*) Medical use, but whether with or without physician's sanction not stated | 61 | 60 | 37 | 52 | 39 | 24 | 32 |
| (*f*) "Patent" medicines | 13 | 12 | 11 | 12 | 10 | 11 | 17 |
| 2. Bad company and dissipation | 14 | 17 | 11 | 30 | 11 | 11 | 11 |
| 3. Degeneracy, hereditary, neurotic temperament, etc. | 9 | 10 | 7 | 10 | 7 | 7 | 8 |

NOTE.—One hundred and fifty-one physicians replied to the questions submitted, but some did not answer all of the questions; others replied to several phases of the same question.

RÉSUMÉ OF REPLIES BY SANITARIUMS TREATING ADDICTION LOCALLY.

*Question 1.*

| | Opium | Morphine | Diacetyl-morphine | Cocaine | Chloral | Cannabis Indica | Other Drugs |
|---|---|---|---|---|---|---|---|
| 1. First used remedially: | | | | | | | |
| (*a*) Careless prescribing or using by physicians | 12 | 14 | 10 | 9 | 11 | 10 | 9 |
| (*b*) First used by physician's direction | 3 | 4 | 2 | 2 | 2 | 2 | 2 |
| (*c*) Self-medication | 2 | 2 | 1 | 2 | 2 | 1 | 1 |
| (*d*) Medical use, but whether with or without physician's sanction not stated | 9 | 10 | 11 | 12 | 9 | 5 | 3 |
| 2. Dissipation | 3 | 5 | 2 | 8 | 4 | 4 | 2 |
| 3. "Patent" medicines | 2 | 3 | 2 | 5 | 3 | 3 | 4 |

NOTE.—Twenty-eight sanitariums replied to the questions submitted, but some did not answer all of the questions; others replied to several phases of the same question.

RÉSUMÉ OF REPLIES FROM SANITARIUMS AND INDIVIDUALS TREATING ADDICTION LOCALLY AND IN ABSENTIA OR IN ABSENTIA ONLY.

*Question 1.*

| | Opium | Morphine | Diacetyl-morphine | Cocaine | Chloral | Cannabis Indica | Other Drugs |
|---|---|---|---|---|---|---|---|
| 1. First used remedially: | | | | | | | |
| (*a*) Careless prescribing | 5 | 5 | 3 | 3 | 3 | 3 | 3 |
| (*b*) First used by physician's direction | 4 | 5 | 2 | 2 | 1 | 1 | 1 |
| (*c*) Self-medication | 1 | | | | | | |
| (*d*) Medical use, but whether with or without physician's sanction not stated | 7 | 9 | 6 | 4 | 3 | 1 | 1 |
| 2. Dissipation | 8 | 7 | | 3 | 2 | 2 | |
| 3. "Patent" medicines | | | | 1 | | | |

NOTE.—Eighteen sanitariums replied to the questions submitted, but some did not answer all of the questions; others replied to several phases of the same question.

The form of replies in some instances was so involved as to make the exact meaning of the author difficult of interpretation. The classification adopted in the above tables gives, it is believed, the information submitted in correct manner. Table No. 1, for example, shows that, in the experience of 35 of the 151 medical men replying, careless prescribing and using of morphine by physicians are among the most common causes of enslavement by this drug. The data in this table furthermore show that in a large majority of cases addiction is due to promiscuous use and indiscriminate sale of these drugs. This is amply substantiated by the experience of sanitariums. It requires only a casual review of these tables to become satisfied that predisposition plays a minor part in habituation. The exciting causes are the great factors. In connection with the replies of the sanitariums, it should be remembered that they are in all probability based on the statements of patients, who are prone to charge some doctor with carelessness rather than indiscretion and follies on their own part.

PHYSICIANS.

*Question 2.*—It is commonly reported that the injudicious or incautious use of habit-forming drugs by physicians in the practice of their profession has led to drug addiction in not a few instances.

(*a*) To what extent do you believe these reports to be correct?

| | |
|---|---|
| 1. In every case | 6 |
| 2. In great majority of cases | 7 |
| 3. In most cases | 13 |
| 4. In many cases | 57 |
| 5. In some cases | 22 |
| 6. To a small extent | 19 |
| 7. Reports exaggerated | 8 |
| 8. Reports incorrect | 5 |
| 9. No reply, or reply indefinite | 14 |
| | 151 |

(*b*) In your experience what method of administration will most readily produce addiction?

| | |
|---|---|
| 1. Hypodermic | 89 |
| 2. Mouth (or other avenue) | 32 |
| 3. Physicians' prescriptions | 7 |
| 4. Patent medicines | 4 |
| 5. Spray or snuff (cocaine) | 12 |
| 6. No reply, or reply indefinite | 19 |
| | 151 |

SANITARIUMS TREATING LOCALLY.

*Question 2.*—(*a*)

| | |
|---|---|
| 1. 90 per cent. of cases | 1 |
| 2. To a large extent | 13 |
| 3. Reports correct | 4 |
| 4. 10 to 20 per cent. of cases | 4 |
| 5. Not to great extent | 3 |
| 6. Reports exaggerated | 1 |
| 7. Reports incorrect | 1 |
| 8. No reply | 1 |

(*b*)

| | |
|---|---|
| 1. Hypodermic | 21 |
| 2. Medicated soft drinks | 2 |
| 3. By mouth | 1 |
| 4. By inhalation | 1 |
| 5. By insufflation | 1 |
| 6. "Self-administration" | 1 |
| 7. "Form in which first administered" | 1 |
| 8. No reply | 3 |

SANITARIUMS TREATING IN ABSENTIA.

*Question 2.*—(*a*)

| | |
|---|---|
| 1. 90 per cent. of cases | 2 |
| 2. 75 to 80 per cent. of cases | 4 |
| 3. 50 to 75 per cent. of cases | 2 |
| 4. To a great extent | 3 |
| 5. Reports correct | 3 |
| 6. In a small percentage of cases | 4 |

(*b*)

| | |
|---|---|
| 1. Hypodermic | 13 |
| 2. By mouth | 2 |
| 3. Hypodermic and by mouth | 1 |
| 4. Reply equivocal | 1 |
| 5. No reply | 1 |

In connection with portion (*a*) of this question, it seems hardly necessary to state that the evidence clearly establishes the correctness of the reports. Portion (*b*) again emphasizes the prominent part played by the hypodermic needle. Thirty years ago this question, in connection with morphine alone, attracted so much attention that Dr. H. H. Kane[2] published a book on the subject. It was considered a great advance in medicine when Dr. Alexander Wood, of Edinburgh, announced, in 1855,[3] the discovery of a subcutaneous method of administering drugs. Its great value in medicine cannot be overestimated. It is undoubtedly true that its use has been much abused, but this is no reason whatever for condemning a method which is employed to such great advantage by the best physicians. In order to indicate the conditions obtaining about thirty years ago I will make some extracts from Dr. Kane's book, referred to above.

"The danger of contracting this habit from the hypodermic use of morphia was recognized[4] in the very infancy of the practice, but was scoffed at or disregarded until a few years ago, when the profession in Germany, England and America awoke, almost simultaneously, to a knowledge of the fact that the habit had become alarmingly common, and that it had been contracted, in the majority of instances, through the carelessness of the physician, who had taught either the patient or his friends how to use the instrument" (p. 267).

"Bartholow, from whose excellent little work I have so often quoted, says:[5] 'The introduction of the hypodermic syringe has placed in the hands of man a means of intoxi-

[2] The Hypodermic Injection of Morphine; Its History, Advantages and Dangers, 1880.

[3] Edinburgh Medical and Surgical Journal, 1855.

[4] Anstie, Practitioner, 1860.

[5] The Hypodermic Method, etc., p. 90.

cation more seductive than any which has heretofore contributed to his craving for narcotic stimulation. So common now are the instances of its habitual use, and so enslaving is the habit when indulged in by this mode, that a lover of his kind must regard the future of society with no little apprehension. It may well be questioned whether the world has been the gainer or the loser by the discovery of subcutaneous medication. For, every remote village has its slave, and not unfrequently several, to the hypodermic syringe, and in the larger cities men in business and in the professions, women condemned to a life of constant invalidism, and ladies immersed in the gayeties of social life, are alike bound to a habit which they loathe, but whose bonds they are powerless to break. Lamentable examples are daily encountered, of men and women, regardful only of the morphia intoxication, and indifferent to all the duties and obligations of life, reduced to a state of mental and moral weakness most pitiful to behold! Usually the habit is formed in consequence of the legitimate use of the hypodermic syringe in the treatment of disease. Employed in chronic painful maladies for a long period, it is discovered, when an attempt is made to discontinue the injections, that the patient cannot or will not bear the disagreeable, even painful, sensations which now occur. More frequently, when the injections are to be used for a long time, the patient is unwisely intrusted with the instrument, and taught all the mysteries of the solutions and the mode of administration.' "

From present observation, it is clearly evident that the situation has not improved.

*Question 3.*—(*a*) In your experience, do you recall any instance in which the use of a patent or proprietary medicine has led to drug addiction?

(*b*) How many such instances?

(*c*) Name of preparation or preparations?

(*a*) PHYSICIANS.

| | |
|---|---|
| 1. Yes | 88 |
| 2. No | 48 |
| 3. No reply, or reply indefinite | 15 |
| | 151 |

(*b*) Only 39 physicians replied definitely to this question. Some reported having observed "many," others "some," and still others "a few." The number of instances seen by these physicians was 217 or more.

(*c*) Many proprietary remedies were given, and for convenience they are classed under the following heads: chloral preparations; headache mixtures containing acetanilide, antipyrine, acetphenetidin, codeine, etc.; soft drinks containing cocaine and caffeine or caffeine only; alcoholic beverages containing cocaine; carminatives, anodynes and in general opium-, morphine- and cocaine-bearing products.

(*a*) SANITARIUMS, LOCALLY.

| | |
|---|---|
| 1. Yes | 22 |
| 2. No | 2 |
| 3. Not able to state | 2 |
| 4. No reply | 2 |

(*b*) About 450 instances.

(*c*) The preparations enumerated are covered by the following heads: soothing syrups; chloral-bearing products; headache remedies; catarrh snuffs;

diarrhœa remedies; anticholera preparations; cough syrups; rheumatism remedies; soft drinks containing cocaine and caffeine; the so-called morphine and opium cures.

(*a*) SANITARIUMS, ABSENTIA.

| | |
|---|---|
| 1. Yes | 15 |
| 2. No | 2 |
| 3. Reply indefinite | 1 |

(*b*) About 31 such instances.

(*c*) The proprietary remedies enumerated by the absentia treating sanitariums are virtually the same as those given by the sanitarium treating locally.

The above clearly shows the part these remedies play in drug enslavement and the need for greater supervision.

*Question 4.*—(*a*) In your opinion, is drug addiction increasing, stationary or decreasing in case of each of the drugs named below?

(*b*) Give reason for the change in each case.

(*a*) PHYSICIANS.

| | Opium | Morphine | Diacetyl-morphine | Cocaine | Chloral | Cannabis Indica | Other Drugs |
|---|---|---|---|---|---|---|---|
| Increasing | 33 | 54 | 35 | 58 | 13 | 10 | 25 |
| Decreasing | 37 | 28 | 12 | 25 | 28 | 16 | 15 |
| Stationary | 16 | 14 | 7 | 8 | 11 | 9 | 6 |

No definite reply in regard to any of these drugs—43.

(*b*) Among the reasons for *increase* given were increased nerve tension and insomnia due to modern strenuous life, inefficient laws, and careless prescribing and dispensing by physicians and druggists.

For *decrease,* restrictive legislation, education of the people, decrease in the extent of the alcohol habit, and the exercise of greater caution by physicians and druggists in ordering and dispensing habit-forming drugs.

(*a*) SANITARIUMS, LOCALLY.

| | Opium | Morphine | Diacetyl-morphine | Cocaine | Chloral | Cannabis Indica | Other Drugs |
|---|---|---|---|---|---|---|---|
| Increasing | 10 | 19 | 16 | 17 | | 1 | 2 |
| Decreasing | 8 | 2 | 1 | 7 | 10 | 7 | 7 |
| Stationary | 3 | 3 | 1 | | 5 | 2 | 2 |

(*b*) Among the reasons for *increase* given were the ease with which these drugs may be obtained by the laity, increasing use of patent and proprietary medicines, greater exposure to temptation, strenuous life, accident and misfortune, panics, illness, disease, etc.

For *decrease,* restrictive legislation, greater caution on the part of physicians in prescribing, effect of Food and Drugs Act upon patent and proprietary medicines, etc.

(*a*) SANITARIUMS, ABSENTIA.

| | Opium | Morphine | Diacetyl-morphine | Cocaine | Chloral | Cannabis Indica and Other Drugs |
|---|---|---|---|---|---|---|
| Increasing | 7 | 12 | 6 | 7 | 4 | 3 |
| Decreasing | 3 | 1 | 4 | 1 | 4 | 1 |
| Stationary | 6 | 5 | 3 | 5 | 1 | 2 |
| No reply | 2 | | 5 | 5 | 9 | 12 |

(*b*) Among the reasons for *increase* given were careless prescribing by physicians, allowing the patient to know what he is taking, desire for dissipation, ease with which these drugs can be obtained, increasing sale of patent and proprietary medicines, instability of nervous system, increase in population.

One party says *all decreasing* because of "pure food law" and education.

It is clearly evident that drug addiction is increasing in the case of cocaine, diacetylmorphine, morphine, opium and "other drugs," and decreasing in the case of cannabis indica and hydrated chloral. The reasons given for the increase and decrease respectively are interesting.

*Question 5.*—(*a*) In your experience, what occupations have furnished the largest quota of drug habitués?

(*b*) About what per cent. of all habitués who have come under your observation have followed each of these occupations?

(*a*) PHYSICIANS.

| | | | |
|---|---|---|---|
| Physicians | 71 | Pharmacists | 31 |
| Prostitutes | 18 | Nurses | 12 |
| Unemployed | 11 | Housewives | 11 |
| "Brain workers" and "professional men" | 9 | Clergymen | 7 |
| Sporting class | 7 | Lawyers | 7 |
| Laborers | 4 | Clerks | 6 |
| Theatrical people | 3 | Artists | 4 |
| Teachers | 3 | Bartenders | 3 |
| Dentists | 2 | Business men | 3 |
| Traveling men | 2 | Printers | 2 |
| Farmers | 2 | Domestics | 2 |
| Skilled mechanics | 1 | Journalists | 2 |
| Photographers | 1 | Cigarmakers | 1 |
| Literary men | 1 | Dressmakers | 1 |
| Railway men | 1 | Brokers | 1 |
| Criminals | 1 | Hotel employees | 1 |
| Barbers | 1 | Students of medicine and pharmacy | 1 |
| Female hairdressers | 1 | Artisans | 1 |
| Spinsters | 1 | Soldiers | 1 |
| Singers | 1 | Drivers | 1 |

Forty-one physicians did not reply to this question.

(*b*) The replies to this question were unsatisfactory. Only a few physicians submitted definite data.

SANITARIUMS, LOCALLY.

*Question 5.*—What per cent. of the drug habitués who have come under your observation have belonged to each of the following classes?

(*a*)

| | PER CENT. |
|---|---|
| Physicians | 35.22 |
| Business men | 16.41 |
| Pharmacists | 5.40 |
| Lawyers | 5.04 |
| Clergymen | 3.18 |
| Artisans | 2.68 |
| Laborers | 1.70 |
| Farmers | 1.35 |
| Other occupations | 28.88 |

(*b*)

| | PER CENT. |
|---|---|
| Males | 65.70 |
| Females | 34.30 |

SANITARIUMS, ABSENTIA.

*Question 5.*—What per cent. of the drug habitués treated by you have belonged to each of the following classes?

(*a*)

| | PER CENT. |
|---|---|
| Business men | 15.33 |
| Farmers | 14.14 |
| Physicians | 13.30 |
| Laborers | 8.76 |
| Artisans | 8.34 |
| Lawyers | 3.80 |
| Pharmacists | 2.47 |
| Clergymen | 2.23 |
| Other occupations | 30.54 |

(*b*)

| | PER CENT. |
|---|---|
| Males | 45.60 |
| Females | 54.40 |

Physicians head the list in the first two reports and are quite well represented in the absentia treatments. Why this unfortunate condition should obtain is rather paradoxical. The physician, of all men, should shun such enticements, knowing as he does the action and power of these agents. It appears to be the old story of familiarity breeding recklessness. The pharmacist also is well represented, and similar remarks are applicable in his case.

*Question 6.*—In your opinion, can addiction due to one or more of the drugs named below be successfully treated by medicine and advice sent through the mail: Opium, morphine, diacetylmorphine, cocaine, hydrated chloral, cannabis indica, and other habit-forming drugs?

PHYSICIANS.

| | |
|---|---|
| No | 139 |
| Possibly in rare cases | 3 |
| "Chloral, yes; morphine and diacetylmorphine, sometimes; the rest, no" | 1 |
| "Opium, morphine and diacetylmorphine, yes; cocaine and chloral, no" | 1 |
| No reply or reply indefinite | 7 |
| | 151 |

SANITARIUMS, LOCALLY.

| | |
|---|---|
| No | 24 |
| Very small percentage | 2 |
| Very doubtful | 2 |

The few exceptions prove the rule.

*Question 7.*—To what extent in your opinion is the immediate supervision of a physician necessary in the successful treatment of addiction caused by the drugs enumerated in Question 1?

PHYSICIANS.

| | |
|---|---|
| Immediate supervision of physician necessary | 128 |
| Necessary in almost all cases | 7 |
| Necessary in most cases | 3 |
| "Opium, 10 per cent.; morphine, 10 per cent.; diacetylmorphine, 15 per cent.; cocaine, 5 per cent.; hydrated chloral, 100 per cent.; cannabis indica, 100 per cent." | 1 |
| No reply or reply indefinite | 12 |
| | 151 |

SANITARIUMS, LOCALLY.

| | |
|---|---|
| Immediate supervision of physician necessary | 28 |

SANITARIUMS, ABSENTIA.

| | |
|---|---|
| Immediate supervision of physician necessary | 2 |
| Immediate supervision of physician not necessary | 5 |
| Necessary only in exceptional cases | 8 |
| Not necessary, but desirable | 3 |

As would naturally be expected, the absentia treating sanitariums differ materially on this point from physicians and sanitariums treating under supervision.

*Question 8.*—To your knowledge is there any known substance or mixture of substances which can of itself remove the craving and cure addiction in case of each of the drugs named below? If so, give name or names. Opium, morphine, diacetylmorphine, cocaine, hydrated chloral, cannabis indica and other habit-forming drugs:—

PHYSICIANS.

| | |
|---|---|
| No | 141 |
| Yes | 1 |
| "Opium, morphine, diacetylmorphine, *hyoscine*, probably exceptionally; rest, no" | 1 |
| Hyoscine hydrocarbonate in case of opium | 1 |
| Possibly (in case of opiates) strychnine and vigorous excretion | 1 |
| "There seems to be a treatment which is successful in case of opium" | 1 |
| Opium, morphine, diacetylmorphine, cannabis, and other habit-forming drugs, yes; cocaine and chloral, no | 1 |
| No reply, or reply indefinite | 4 |
| | 151 |

SANITARIUMS, LOCALLY.

| | |
|---|---|
| No | 27 |
| No reply | 1 |

What might be called the Towns-Lambert[6] treatment has been designated as "specific" by Dr. Lambert, and he reports excellent results; but, unfortunately, other observers do not confirm his findings. Charlatans healing in absentia usually assuage the cravings by giving liberal doses of the very drug

[6] Journal of the American Medical Association, vol. liii, p. 985, 1909.

the habit of which they profess to eradicate. The much-advertised "combretum" plant antidotal treatment for opium does not appear to have many advocates.

*Question 9.*—In your opinion does the present form of legislation restricting the sale of habit-forming drugs materially check their use by habitués?

PHYSICIANS.

| | |
|---|---|
| Yes | 32 |
| To a large extent | 6 |
| To a limited extent | 30 |
| Yes, except morphine | 1 |
| No | 64 |
| No, except cocaine | 2 |
| No reply, or reply indefinite | 16 |
| | 151 |

SANITARIUMS, LOCALLY.

| | |
|---|---|
| Yes | 4 |
| To a limited extent | 6 |
| No | 14 |
| No, except cocaine | 1 |
| Not able to say | 3 |

The present form of legislation, which carries with it the enforcement of the laws, apparently does not give satisfactory results.

SANITARIUMS, ABSENTIA.

*Question 7.*—Please describe briefly in space below the method of treatment employed and recommended by you.

| | |
|---|---|
| Rapid withdrawal | 2 |
| Gradual | 10 |
| Rapid or gradual, according to circumstances | 1 |
| General, supporting treatment | 1 |
| Reply indefinite | 3 |

*Question 8.*—In your experience what has been the average length of time which has elapsed between the beginning of the treatment and the complete and final withdrawal of the drug?

| | |
|---|---|
| Immediate withdrawal | 1 |
| One to three months | 3 |
| Three to six months | 4 |
| Six to nine months | 2 |
| Nine to twelve months | 2 |
| "Several months" | 1 |
| Reply irrelevant | 3 |
| No reply | 2 |

*Question 9.*—In what per cent. of cases has your treatment resulted in the complete eradication of the habit?

| | PER CENT. | |
|---|---|---|
| 1. | 23.5 | |
| 2. | 30 | |
| 3. | 35 | |
| 4. | 40 | |
| 5. | 50 | (Average, 53.85 per cent.) |
| 6. | 60 | |
| 7. | 75 | |
| 8. | 75 | |
| 9. | 75 | |
| 10. | 75 | |
| 11. Large percentage of cases | | 3 |
| 12. No records | | 2 |
| 13. No reply | | 3 |

*Question 10.*—What are the most important reasons for the failure of your method in the cases which resulted unsuccessfully?

| | |
|---|---|
| 1. Failure to follow directions | 6 |
| 2. Lack of co-operation | 3 |
| 3. Lack of will-power | 3 |
| 4. Financial disability; giving up treatment too soon | 3 |
| 5. Intercurrent diseases | 3 |
| 6. Lack of restraint | 1 |

SANITARIUMS, LOCALLY.

*Question 11.*—What form of addiction, as regards kind of drug, most frequently comes under your observation?

| | |
|---|---|
| Morphine | 19 |
| Morphine and cocaine | 4 |
| Morphine and opium | 1 |
| Opium and derivatives | 1 |
| No reply | 3 |

SANITARIUMS, ABSENTIA.

*Question 11.*—What form of addiction, as regards kind of drug, is most frequently treated by you?

| | |
|---|---|
| Morphine | 10 |
| Opium and morphine | 4 |
| Opium and derivatives | 1 |
| Reply indefinite | 1 |
| No reply | 2 |

This information clearly shows that morphine supplies by far the greatest quota of inmates of these institutions.

SANITARIUMS, LOCALLY.

*Question 12.*—If possible, will you state how many instances of addiction, in case of each of the drugs enumerated below, came under your observation during the years 1906, 1907 and 1908?

| Year | Opium | Morphine | Diacetyl-morphine | Cocaine | Chloral | Cannabis Indica and Other Drugs |
|---|---|---|---|---|---|---|
| | *13r | 18r | 7r | 15r | 7r | 11r |
| 1906 | 42 | 458 | 16 | 75 | 9 | 23 |
| 1907 | 62 | 564 | 9 | 120 | 5 | 23 |
| 1908 | 66 | 604 | 17 | 127 | 9 | 47 |

*r, replies.

SANITARIUMS, ABSENTIA.

*Question 12.*—If possible, will you state how many instances of addiction, in case of each of the drugs enumerated below, were treated by you in the following years: 1906, 1907 and 1908?

| Year | Opium | Opium and Morphine | Morphine | Morphine and Cocaine | Diacetylmorphine | Cocaine | Chloral | Cannabis Indica | Other Drugs |
|---|---|---|---|---|---|---|---|---|---|
| 1906 | 116 | 320 | 796 | 4 | 2 | | | | |
| 1907 | 93 | 290 | 819 | | 2 | 14 | 1 | | |
| 1908 | 80 | 242 | 523 | | 2 | | | | |

NOTE.—Summary based on 7 replies, the remaining 11 being indefinite.

The number of cases treated with supervision and possibly restraint is increasing, whereas absentia treatment cases are apparently decreasing. What are the reasons for the decrease in the latter? Are publicity and failure to give satisfaction, factors?

SANITARIUMS, LOCALLY.

*Question 13.*—If possible, will you state how many instances of addiction you now have under observation in case of each of the drugs named below:—

| | | | | | |
|---|---|---|---|---|---|
| Opium | 16 | Diacetylmorphine | 3 | Cannabis indica | 0 |
| Morphine | 203 | Cocaine | 36 | Other habit-forming drugs, drugs not stated | 11 |
| Opium and morphine. | 5 | Chloral | 2 | | |

SANITARIUMS, ABSENTIA.

*Question 13.*—If possible, will you state how many instances of addiction you now have under treatment in case of each of the drugs named below:—

| | |
|---|---|
| Opium | 89 |
| Morphine | 460 |
| Morphine and chloral | 1 |
| Diacetylmorphine | 27 |
| Cocaine | 5 |
| Chloral | 1 |
| Cannabis indica | 0 |
| Other drugs | 0 |
| Miscellaneous (drugs not stated) | 187 |
| | 770 |

Morphine, as usual, heads the list. Cocaine habitués apparently do not submit themselves to treatment in proportion to the prevalence of the evil.

NOTE.—Summary based on 6 replies; remaining 12 indefinite.

*Question 14.*—Can you suggest any measures, legislative or otherwise, which might be put into effect to eradicate drug addiction?

SANITARIUMS, LOCALLY.

Among the measures suggested are the following: Make sale illegal and prohibitive; enforce present laws; pass more rigid federal laws; pass laws prohibiting sale of home treatments; pass laws to confine habitués to institutions; educate the public, particularly the young. One party suggests: Make it perfectly easy to secure these drugs; this would do away with secret drug-using.

PHYSICIANS.

Among the suggestions offered are the following (the order indicates the importance of the suggestion, those emphasized by the greatest number of physicians appearing at the head of the list) :—

1. Enact stringent legislation permitting the sale of habit-forming drugs upon physician's prescription only.
2. Prohibit by law the refilling of prescriptions except on physician's order.
3. General education of the public, particularly the young.
4. Provide Government and State institutions for habitués.
5. Stimulate physicians and pharmacists to greater efforts at prevention of drug habits.
6. Make illegal sale a penal offense.
7. Continue present laws as to labelling.
8. Banish from trade all patent and proprietary medicines containing habit-forming agents.
9. Permit sale of habit-forming drugs to physicians in person only.
10. Publish prescriptions giving name of user.
11. Revoke license of physicians and pharmacists known to be habitués.
12. Enact legislation requiring physicians and druggists to present to the authorities at stated intervals reports as to the quantity of each habit-forming drug prescribed or dispensed by them.
13. "Governmental supervision and distribution through physicians only."
14. Stop counter-prescribing by pharmacists.
15. "Absolute stifling of all channels of publicity for the sale of nostrums and proprietaries."
16. "Have every prescription for these drugs turned over to the police, or give them the right to inspect prescription files and make provision for care of those given to the habit."
17. Prosecute physicians prescribing an undue quantity of these drugs.
18. Kill off habitués.
19. Legalize unsexing of habitués.

Comments on the foregoing seem to be unnecessary.

DISCUSSION.

*Dr. Fisher* asked Dr. Kebler how this country stood as compared with England, Russia and other great countries as regards the proportionate number of drug habitués?

*Dr. Wilcox* said that the work of investigation done by Dr. Kebler deserved the highest commendation. The checking of the sources of drug addiction is in the line of conservation of the resources of the country. We have heard much of late about the necessity for such conservation; every drug habitué represents just so much loss to the community and the country, and anything which tends to check the spread of drug addiction tends just so much toward the conservation of our national resources. The subject, he thought, should be considered in this light.

*Dr. Stewart* said that the efforts of the government have already been productive of great good. Manufacturing and other pharmacists never before appreciated as they

do now the dangers which attend the promiscuous sale of preparations containing habit-forming drugs. A great change in sentiment has taken place throughout the entire country with regard to the indiscriminate sale of these agents.

*Dr. Osborne* discussed the various treatments which are used for the cure of drug addiction. Almost every drug in the materia medica has been tried in an endeavor to find some agent which will of itself do away with the craving for stimulation, but none such has as yet been found. Many of the treatments depend for their alleged efficacy upon the presence of hyoscine, belladonna or stramonium. One of them, to which allusion has been made, contains atropine, which, in the carrying out of the treatment, is pushed to toleration, and the limit of toleration is placed high by active purging to the point of prostration; so that, between the prostration due to the purging and the stimulation to distraction caused by the atropine, the victim does not know what he wants.

On motion of Dr. F. H. Gerrish, Portland, Maine, the thanks of the society were extended to Dr. Kebler.

*Dr. Gerrish* said that for thirty-five years he had been interested in the suppression of alleged cures for the drug habit. His county medical society investigated twelve of these so-called cures many years ago, and found that the method generally employed by the advertising concerns was first to ascertain by correspondence how much of the drug the patient was accustomed to take daily, and then to increase this dose a little in the "cure." A more hellish scheme for fastening the victim's chain more securely upon him could not be devised. The analyses of the medicines comprising the treatments were made by Dr. Squibb gratuitously, and there was no question as to their accuracy. The results were sent to every editor and clergyman in the State, and were given publicity in every way. Unfortunately, however, the society was not able to keep up the campaign indefinitely, and the concerns continued to do business. At the meeting of this society three years ago he had advocated as essential to the cure of the drug and alcohol habit the enactment of legislation by which any adult who desires to be cured of his habit can voluntarily relinquish his liberty for ninety days to a properly authorized physician. That provision now stands as a law in Maine.

*Dr. Kebler,* in reply to Dr. Fisher's question, said that drug addiction is much less prevalent in some of the European countries than in the United States; perhaps not in England, but in Germany, Holland, Italy and Spain. The Philippine Islands have the most drastic anti-opium law of any country.

Drug cures, he said, were a delusion and a snare. His department has been investigating about thirty of these treatments, and he hoped he would soon be able to publish the results. A number of our present laws do not reach these concerns. One of the treatments contains twenty-two, and another twenty-four grains of morphine, per ounce; others contain cocaine, and some of them cannabis indica. Some depend on the gradual reduction plan, and the reduction is gradual indeed,—something like a quarter of a grain a month in one instance. As a matter of fact, the promoters do not, as a rule, have the welfare of the unfortunate victim at heart.

# U. S. P. 1910. HOW MAY IT BE CONSTRUCTED?

By O. T. OSBORNE, M.A., M.D.,
Professor of Materia Medica, Therapeutics and Clinical Medicine
in the Yale Medical School,
NEW HAVEN, CONN.

I HAVE been asked by our President to open this discussion on the Pharmacopœia of 1910. To further this request, it seems to me I can do no better than to elucidate my propositions already in print, the first one being:—

1. Let the new Pharmacopœia contain such drugs only as are of positive therapeutic value.

If we are in the age of scientific beliefs and research, I cannot see how this preamble can be objected to by anyone. Certainly no one individual practitioner wishes to perpetuate a drug he considers valueless, or would use one for a specific purpose that he deemed valueless. In the abstract, then, no one could object to this resolution. Now, as to what drugs are valueless. Here comes the crux of the whole discussion and perhaps the Waterloo of failure, and nothing will save the recommendation but to carry the opposition by the storm of proposition No. 2, viz.:—

2. When a drug or preparation of a drug is prescribed that is not official in the Pharmacopœia of 1910, let it be officially declared that the standard of purity and the methods of making preparations not recognized in the Pharmacopœia of 1910 be the standard set, and the methods of preparation ordered in the last Pharmacopœia in which the preparation was recognized.

There is absolutely no satisfactory outcome to be expected from any circulation of requests for approval or disapproval of the various drugs contained in the present Pharmacopœia. The differences of opinion would be legion, and the slim majority obtained for deletions of little practical value. Such decision for deletion must be left to the judgment of from three to five clinical men selected by the U. S. P. Revision Committee. Practitioners all over the United States who are disappointed by these omissions from the U. S. P. of 1910 may regret and pity the lack of wisdom of this deletion committee, but must be therapeutically and pharmacally content with the U. S. P. 1900 standard for their pet drugs. If a deleted drug is valueless, how can a certification to that fact be better made than by omitting it from the 1910 Pharmacopœia? If a deleted drug is of value, it will survive in spite of such deletion, and may be incorporated into the 1920 Pharmacopœia, as any new drug found valuable.

3. Let the 1910 Pharmacopœia contain such new drugs as have been proved of therapeutic value.

All honest practitioners of medicine must approve of this recommendation. A drug (not some fool-befogged formula to cloud the active ingredient) that is of value in overcoming disease or a disturbed condition, whatever the source from which it was derived, or by whom discovered, should be made official.

And here again a committee of five clinicians appointed by the U. S. P. Revision Committee must decide what drugs are eligible, and then what drugs are of sufficient therapeutic use to be officialized. Again, many will not be satisfied with the committee's selection, but a drug found valuable and not recognized by the committee will be in no worse position than it was before, viz., an unofficial drug. Such a drug will clamor for recognition, and may be recognized by recommendation No. 4. On the other hand, if a drug is raised to importance and prominence unadvisedly by this committee, or if another similar-acting and better drug has been discovered and supersedes it, it may be dropped from the U. S. P. of 1920, and then each Pharmacopœia will represent scientific advance and not, as now, be a book of historic reference.

Recommendation No. 4 is as follows, and needs no discussion, except as a question of advisability and policy:—

4. Let there be issued a supplement to the Pharmacopœia, in 1915, which shall make official such new drugs as have been proved to be of therapeutic value during the years of 1910 to 1915.

5. Let the 1910 Pharmacopœia give the most simple titles possible to all new drugs, especially to the synthetic drugs. If it is considered impossible or inadvisable to make an official title of a drug simple, an official abbreviation should follow the name of the drug. Every writer of a prescription, and most assuredly every teacher of materia medica and prescription-writing, will approve of this. The terrible, heart-rending and brain-splitting attempt to prevent all possible advertisement of a proprietary drug has been followed by continuous damning all over this country, and has forced the ordering of the drug by its proprietary name, much to the profit of the drug promotor.

6. Let it give official approval to only the best of the preparations of the official Galenic drugs, and not officialize the little-used and useless preparations of these drugs.

In the abstract everyone must approve of this as read. Now, again, who shall determine which are the most efficient preparations? Why not a committee of ten, five clinicians and five pharmacists, appointed by the Revision Committee? Whatever this committee decides, it will be damned anyway. But it is certainly supposable that one or two preparations of a Galenic drug are better than the others, and certainly the best is none too good. Again, if a prescriber desires a deleted preparation, he can revert to the 1900 Pharmacopœia. But a smaller, useful teaching book we must have for medical school purposes.

7. Let it not give official approval of all of the known salts (of iron and mercury, for instance), but only of the best.

This is similar to recommendation No. 6, and should be decided by the same committee, and their decision will be subjected to the same berating. It might even be well for this committee to be protected by special insurance policies against suits for malfeasance in office. All joking aside, it is perfectly supposable that some few salts are better than many other salts, and again comes up the advisability of reducing the unnecessary number of official preparations to what can be readily taught to medical students as the best.

8. Let the average adult dose appear after each drug and each preparation of it, not the range of dose, *i.e.*, minimum to maximum, as there is no exact under- or over-limit of dose. The dose is enough to accomplish the object aimed at by the prescriber, and all he cares to know is the average dose.

This recommendation is self-explanatory. It certainly cannot be dictated how small a dose a prescriber may order. Nor should he be officially limited to a given dose when, in his judgment, with a particular preparation, in a particular condition, in a particular patient, a larger dose is required. Chemical assayists and pharmacologists attest to the varying strength of drugs and preparations, and this will perhaps be always true of Galenic drugs. Consequently, it is absurd to prescribe dogmatically the limit of dosage, or to give such a wide range of dosage as to make the drug and its strength appear ridiculous. Let there be no translation of metric to Troy doses. Let each dose (and both should be given) be smooth for each system.

9. As the U. S. P. gives the official titles of drugs in Latin, it should also give the genitive after each title. This would be of special value in teaching the correct writing of prescriptions. It is not always easy to determine the declension to which a Latin noun belongs, or whether it may not be indeclinable.

This cannot well be objected to by anyone, and will be a real help to teachers of medical Latin and to medical students.

10. Let the official preparations of a drug be enumerated under the title of that drug.

This was an omission from the last Pharmacopœia that has been considered a mistake, and I doubt not that the next Revision Committee will be glad to rectify it.

In closing, let me express the hope that a vote by this Society on each recommendation will be transmitted to the new Revision Committee. A positive vote will help the Committee, and a negative vote will show that a body of clinicians cannot back up the recommendation.

## DISCUSSION.

*Dr. Wiloox* said that all of us who had given much thought to the subject agreed with the views expressed by Dr. Osborne. The majority of the opinions which he himself had held ten years ago he still held to-day. The difficulty of realizing his theories for the Pharmacopœia of 1900, however, had soon become apparent. To Professor Good and himself was delegated the work of recommending to the Revision Committee the drugs which should be added to and those which should be dismissed from the Pharmacopœia. The method to be employed in securing information upon this subject was left to their discretion. Accordingly, he sent out circular letters to the American Medical Association and its affiliated bodies and to all State and county medical societies and national special organizations, requesting information as to what drugs in the opinion of these bodies should be dismissed from and which should be added to the Pharmacopœia of 1900. He failed to receive a reply of any kind from the American Medical Association, and not a suggestion had he ever received from it. The medical societies of the States of New York and Connecticut furnished valuable information, as did also those of Louisiana and one or two other States. Repeated inquiries, extending over a period of four years, failed, however, to elicit any opinion which could be called representative from the medical profession upon the question at issue. Professor

Good, who investigated the same matter from the standpoint of the pharmacist, succeeded in finding out, largely from druggists' files, what medicines were most prescribed by physicians, and by their joint efforts they made a report and submitted it to the Committee on Revision. He then began to think just about as Dr. Osborne does, and he would end his term of service with the same views, namely, that nothing can be gained by attempting to obtain information for the Pharmacopœia through the agency of circular letters. Some of the most severe and unjust of the criticisms which were directed against the last Pharmacopœia came from those who had refused to give any opinion or suggestion relative to the work when they were consulted. How shall we succeed in making the Pharmacopœia a representative work for physicians if the medical profession is going to remain silent at such times? Personally, he would be glad to see every one of Dr. Osborne's suggestions adopted by the Revision Committee. He would like to see an intelligent board composed of medical men appointed to determine just what drugs, from a clinical standpoint, should be added to and which ones should be dismissed from the Pharmacopœia. The report of such a board would have great weight with the Revision Committee.

*Dr. Dawes* said he not only believed in the wisdom of Dr. Osborne's suggestions, but he also hoped that they would prove more practical than Dr. Wilcox had indicated. It was a fact that not more than one physician in a hundred owned a Pharmacopœia, or knew what was in it. Teachers of materia medica and therapeutics, of course, must have it, but the great majority of physicians were unfamiliar with it. He believed, however, that a change had gradually been coming over the country, and that physicians had been shaking off their lethargy and indifference toward matters pertaining to the Pharmacopœia. The awakening was largely due to the effect of Dr. Osborne's published articles. He did not think the negligence of which the American Medical Association was guilty in 1900, in not replying to the inquiries of Dr. Wilcox, would obtain at the present time, and he expressed the belief that the present Revision Committee would experience no difficulty in this direction. He hoped that the society would adopt and recommend all of Dr. Osborne's suggestions.

*Dr. Dawes* then moved the adoption of the suggestions by the society, and, the motion having been seconded and passed, he was requested by the Chair to write out the suggestions and present them seriatim for the action of the society.

*Dr. Stewart* expressed the opinion that Dr. Osborne's suggestions were thoroughly in accord with the most advanced ideas as to what the new Pharmacopœia should contain.

*Dr. Wilcox* said that there is not an agent in the Pharmacopœia which has not been and is not now being prescribed by physicians. This is true of drugs which most of us believe to have been relegated to obscurity. The country is large, and drugs which are used in one section are not necessarily used in another at all. The physician in the West has the same right to his opinions as his brother in the East, and it is important to bear this in mind in deciding upon the drugs which should be dismissed from the Pharmacopœia. Care should therefore be taken that a board like the one suggested should be thoroughly representative of all sections of the country.

*Dr. Osborne* agreed entirely with Dr. Wilcox as to the futility of attempting to secure opinions relative to the next Pharmacopœia through the agency of circular letters. It was largely on this account that he had suggested the appointment of a representative board to make recommendations to the Revision Committee concerning the preparations which should appear in the Pharmacopœia of 1910.

All the recommendations of Dr. Osborne, with slight modifications in one or two instances, were then adopted, and Dr. Dawes was requested to present them to the U. S. P. Revision Committee as the formal opinion of the society.

# SHOULD THE PHARMACOPOEIA CONTAIN ONLY USEFUL AND EFFICIENT DRUGS?

By N. S. DAVIS, M.D.,
CHICAGO, ILL.

I HAVE served so long upon the Revision Committee of the Pharmacopœia that I appreciate perfectly the view of pharmacists who desire in the Pharmacopœia every substance much used in any part of our country as a medicine, whether it possesses real value or not. However, I believe the time has come when in adding to the Pharmacopœia and in deleting from it we should be guided by the utility of the drug as a medicine. It must be remembered that the Pharmacopœias of all lands and of all times contain a selected list of drugs; to include everything which has been used has never been attempted. Supposed usefulness has always suggested to the makers of these compilations the admission of drugs, and if they have also been much used there has been no hesitation about admitting them.

If the Pharmacopœia is to establish standards for drugs, it is natural to ask what are drugs. A generally admitted definition is, something administered to those who are diseased to aid them to recover health, or to lessen suffering. This implies potency or pharmacological activity. If time, experience and experimentation have shown that any substance formerly used as a drug was valueless, should it be kept in the Pharmacopœia? From successive editions many such substances have been dropped, and in the forthcoming revision we must face the problem of dropping others. Shall we be guided in this by the usefulness of the substance (this appeals to our reason), or continue to establish standards and discover methods of assay for substances which are valueless, or almost so, as drugs, when there are plenty of active valuable ones? In admitting a new drug to the Pharmacopœia should we be guided by any other rule than its utility as a medicine and its superiority to those already in the Pharmacopœia? I am sure you will say, no. And the revision committee will say, no. Why, then, in making deletions should we be guided by a different rule? Many of the drugs of little or no potency still in the United States Pharmacopœia were originally used by the Indians, from whom the early settlers learned to employ them, and later they were adopted by the physicians of earlier times, who could obtain few imported or manufactured drugs and were compelled to use what was at their hand. Moreover, these drugs were generally adopted by the eclectics, which gave them a continued use. Experience and experimentation, however, have proved that many of them possess little or no value, while time has given us others which are more reliable and efficient.

Recently I have received, and I presume most of you have, a digest of the comments and criticisms which have been made upon the present Pharmacopœia. I was surprised to note how few comments have been made during the last five years upon the pharmacological and therapeutic value of these

drugs. What comments of this kind are recorded in this digest pertain almost exclusively to drugs which the best students of therapeutics believe have no, or almost no, value. For example, I find that, in an eclectic journal, berberis aquifolium (which, by the way, is a most interesting shrub in the gardens of those of us who cannot grow holly, of which it reminds one) is commented on thus: "It cures syphilis and skin disease, chronic ulcers, psoriasis and senile bronchitis. Its action is slow, but if persisted in for months it will cure almost anything curable by medicine when it is a question of chronic inflammation of a local character with a tendency to relaxation and breaking-down of mucous membranes." Such fulsome and general commendation damns the drug in the minds of thorough students of pathology and therapeutics. It is to be regretted that the true active principle in the treatment praised so highly can not be admitted to the Pharmacopœia. I refer to *time,* the most potent aid possessed by the clinician. However, we might find it difficult to fix for it a purity rubric. If the best physicians in all lands reject such substances, why should they be retained? Physicians and druggists no longer collect their own simples, and therefore are not dependent upon their neighborhood for supplies. In the most distant corner of the country a rare drug can be gotten almost as easily as a common one, for both must be procured from the importer or manufacturer.

It must be remembered that physicians have as much interest in the Pharmacopœia as druggists, for to them it is most important that the preparations which they use should be standardized; but they need some kinds of information which the pharmacist cares less for, just as he is much more interested in the physical and chemical properties of drugs than the physician is. Physicians need a list of genuinely useful drugs, made by authoritative students of pharmacology and therapeutics; a list which will guide them, instead of the clever advertisements of manufacturers. Ought not the Pharmacopœia too be based upon such a list? Physicians also need to have authoritatively collected the physiological effects of drugs to guide them in applying the latter therapeutically. This information will also interest pharmacists. If drugs are defined by their pharmacological action, as well as by their physical and chemical properties, inert preparations of drugs cannot be safely sold, as they have been in the past. It is quite as possible for a group of well-known students of pharmacology to make such a compilation, and, when necessary, decide conflicting views by experimentation, as it is for a similar group of pharmacists to decide upon assays of drugs.

For the good of physicians and their patients all compounds should be omitted from the Pharmacopœia. The habitual use by physicians of ready-made pills and mixtures makes it impossible for them to adapt doses to the requirements of individual patients or to their varying needs. Moreover, it leads to ignorant prescribing, because it tempts physicians into bad habits of not thinking. I am sure many of those present have had the same experience which I have had in numerous consultations. When I have asked a physician in charge of a patient what he was giving he has replied, "Pill No. 22, made by X. Y. Z.," or given a somewhat similar answer. When I have asked what was

in it he has answered, "I *think* so and so," and, when asked the dose of the drugs, he has replied, "Three or four pills a day." He did not know the dose of the individual drugs in the pills, and was not quite sure of the drugs. If twenty surgeons, who are the chief prescribers of compound cathartic pills, were asked their contents and the doses of their ingredients, I do not believe one-half could answer correctly. They are composed of drugs almost never incorporated in a prescription by physicians. Their continued use has become a hospital habit and does not mean that they are the best thing for the patients. So demoralizing does the habitual use of made-up formulæ become! They are bad for the physician and inimical to the best treatment of patients. A good therapeutist selects drugs and the doses of them to fit the need of each patient. Unless this is done patients are not as well treated as they might be. So long as by ready-made pills the habit of using fixed formulæ is cultivated and confirmed, the practice of medicine in the best way is impossible. Therefore the Pharmacopœia should not contain them. But this is somewhat aside from the topic assigned me. The admission of numerous almost or quite inert substances into the Pharmacopœia is a help to manufacturers of proprietary mixtures, for they can use such drugs safely, and yet advertise that their formula contains only articles in the United States Pharmacopœia. Pharmacists often assert that the Pharmacopœia is not a text-book and is not a treatise on therapeutics, and in almost the same breath they complain because medical teachers do not teach their students especially to use pharmacopœial preparations. How can they, when much that is in the work is inimical to good therapeutics, and when, moreover, some of the drugs in it can only be described as useless or almost so. Under such circumstances can you expect medical men to highly prize the book? Yet it should be as much prized by the physician as by the pharmacist, and is really as essential to the one as to the other.

Lastly, the drugs still included in the Pharmacopœia which are of little or no value are few in number, and, if omitted, would not be missed, any more than those omitted when the Pharmacopœia was last revised are missed to-day. I have not made a careful count of the drugs now in the Pharmacopœia which possess little or no pharmacological activity, but believe that I am not far from right when I estimate them at twenty or twenty-five. The elision of many of them has been recommended by committees of various sections of the American Medical Association. Ought not the Revision Committee of the Pharmacopœia to be guided in omitting old drugs from it by the same rule that will guide them in admitting new drugs to it, namely, that they must have pharmacological activity and be the best of their class?

## DISCUSSION.

*Dr. Stewart* said that dead stock in the Pharmacopœia meant dead stock in the drug stores, and he believed that every pharmacist would heartily endorse Dr. Davis's suggestion that only drugs of some potency and value should be admitted. He also agreed with the speaker as to the desirability of the omission of compounds, like compound cathartic pills, and said he was opposed to the promiscuous prescribing of ready-made mixtures. The only argument which could be advanced in their favor was that

they sometimes supplied a need of the country physician, who did not always have a pharmacy near at hand.

*Dr. Osborne* spoke of some of the "undesirables" of the Pharmacopœia, referring especially to compounds and some of the flavoring agents. He believed that the former should be entirely excluded from the work. The compound cathartic pill, which had been alluded to, was an example of just what we do not want in the book. It contains at least six cathartics, and probably only one of them actually does the work. If one wishes to give calomel, give it; or, if one wishes to give jalap, give it; but do not prescribe five or six cathartics when only one of them is needed. Every student in the Yale Medical School is required to spend at least fifty hours in a city drug store putting up the most important pharmacopœial preparations, watching the filling of prescriptions, and then writing criticisms on what he has observed. According to Dr. Osborne's observation while overlooking this work, the number of fool prescriptions written by city doctors was astonishing. He cited examples, referring particularly to those which contain complex flavoring vehicles. "Why," he asked, "should one use three or four flavoring agents in a single prescription if one will suffice?"

*Dr. Barton* also agreed with Dr. Davis that the Pharmacopœia, to be a practical work for the physician, should contain only drugs of some potency and value. As to his suggestion that this would result in the elimination of about twenty-five drugs, he hoped that it would affect more than this, many more. He favored the introduction of a brief statement of accepted facts relative to the physiological action of each drug, and he hoped that this suggestion would meet the approval of the Revision Committee. If the Pharmacopœia were to be made a practical work for physicians, it should contain this information. Why not do this now? Why wait ten years to do it? One reason why so few physicians own copies of the book is because there is not enough information in it to pay them for buying it. The size of the work would not be materially increased by the addition mentioned if the pages were made a little thinner and the subject-matter condensed.

*Dr. Davis*, in closing, said that the number twenty-five which he had mentioned referred only to those drugs which had no potency or value; he would like to see many more dropped for other reasons.

# REVISION OF THE UNITED STATES PHARMACOPOEIA.

By JOSEPH P. REMINGTON, Ph. M.,
PHILADELPHIA, PA.

THE Convention for revising the United States Pharmacopœia will meet next week, and more interest in its revision will be taken by physicians than ever before, except in the very first years of the life of the Pharmacopœia. That the American Therapeutic Society is aroused from its former state of inactivity as regards this work is proved by the fact that one session in your deliberations is devoted to a "Symposium on Matters Pertaining to the Revision of the United States Pharmacopœia," and ten papers will be read upon pharmacopœial subjects. The greatest difficulty to be encountered in awakening interest in the Pharmacopœia by physicians is the tendency, especially marked among the younger members of the profession, to never use an old remedy in a prescription if they can possibly think of a new one which will answer their purpose. Should not the opposite view prevail? The obliging commercial houses are always ready to take advantage of this tendency to try some new remedy, and the universal hunt for a panacea is always in evidence. While in music, art, and literature something new and fetching must always be provided, the *masterpieces* still live; we never tire of listening to the old operas or of reading the works of the old authors, and in art the old masters still stand pre-eminent. To draw a parallel with reference to the use of drugs and remedies for the treatment of disease seems like an anachronism, but the law of the survival of the fittest applies to everything.

That there is a marked change in the attitude of physicians throughout the country must be apparent to all. Physicians are going back rapidly to the use of pharmacopœial preparations, but the young practitioner is taking up the subject *de novo*. He knows comparatively nothing about the Pharmacopœia, and to him the subject is a mystery. He cannot understand the why and the wherefore for this renaissance. Is this not, almost solely, due to neglect on the part of the professors in our medical schools, who have for years failed to impress upon their students the necessity for studying and using the ethical preparations of the Pharmacopœia, just as the professors and teachers of music, literature and art point to the best examples which have survived the incursions of the newer army of productions? Progress and research, of course, must ever be carried on if life is desired, but until the time arrives when therapeutics attain a condition of greater exactness and accuracy empirical results must be retained.

The controversy which has been going on recently in the medical and pharmaceutical journals, and even in the public newspapers, concerning the scope of the Pharmacopœia has developed two clearly marked opposing views. On the one hand, there is a decided movement to curtail the list of articles to be admitted to the new Pharmacopœia, while, on the other, a powerful counter-

movement has been set on foot to greatly enlarge the number of remedies. Both of these ideas will, no doubt, be ably championed in the coming Convention, but it does not need the vision of a seer or a prophet to foretell that neither extreme will ultimately prevail, and when both sides are heard the next Committee of Revision will undoubtedly admit a selected number of the newest articles and will delete many of the older ones which have, in the eyes of many members of the medical profession, outlived their usefulness. This controversy, which has been carried on in an admirable spirit, largely devoid of bitterness and hard words, has been of great value in clearing the atmosphere, and both physicians and pharmacists, while they will take up their responsibilities with more adequate conceptions of the magnitude of the task before them, will have to guide them a vast amount of information, gathered from all sources. While it will be difficult for the Committee of Revision to always wisely make a proper selection of material, I have the faith to believe that out of the multitude of counsellors there will come wisdom, and that the Ninth Revision of the United States Pharmacopœia will prove to be the best that has been written.

## DISCUSSION.

*Professor Remington* in further pursuing the subject of his paper said that one of the great difficulties that had been encountered in previous revisions of the Pharmacopœia was that those who had been asked to aid in the work of revision naturally gave their own opinions, and they were much controlled and limited by their environment. We should remember, however, that the Pharmacopœia is a work of national significance, and, while each physician naturally has a preference for the remedies which he has tried and found useful, he should bear in mind that physicians in other parts of the country use remedies which he may never have employed. The work is not intended for local use, but to be a guide for physicians and pharmacists all over the country. In Washington or Philadelphia a physician may obtain excellent results from the use of twenty or thirty drugs, and yet is it not possible that a physician in San Francisco may obtain equally good results from twenty or thirty others quite different? One physician may prefer sodium benzoate and another, ammonium benzoate; must either drug necessarily be dropped? We should endeavor, therefore, to regard the Pharmacopœia from a broad point of view. Again, we must remember that it is now a legal standard for drug products all over the United States; so that when a physician prescribes a pharmacopœial remedy, the druggist must give him that particular remedy as prescribed in the Pharmacopœia.

*Dr. Osborne* asked Professor Remington what objection there would be to inserting a provision in the Pharmacopœia to the effect that a drug which had been dropped must comply with the standards which obtained when the drug was last official.

*Professor Remington* replied that the laws of most of the States require that preparations bearing names which appear in the Pharmacopœia must comply with the standards for these articles set forth in the latest edition of the Pharmacopœia. Otherwise, a confusion of standards might arise. This does not, however, prevent the physician from specifying a remedy described in the Pharmacopœia of 1870, 1880, or 1890, for instance, if he so desires. A statement upon the title page of a new Pharmacopœia has the effect of throwing the old Pharmacopœia out of commission, because the time fixed when the old was printed is then superseded.

*Dr. Osborne* said that if we put into the Pharmacopœia everything that physicians want there will be practically no limit to the size of the work. How about the drugs which have already been dropped and which will be dropped? According to Dr. Remington, they are all used by physicians somewhere in the country. What right then have we

to drop any of the official preparations? He could not see why we should not take a decided stand and have a Pharmacopœia containing only those remedies which possess potency and therapeutic value. He wished to have the work up-to-date therapeutically.

*Professor Remington* asked, "Who is to say that this or that drug is valueless?" We have no authority to decide such a question.

*Dr. Osborne* in reply, called attention to his recommendation for a board of representative physicians, who should be authorized to decide these questions and make to the Revision Committee such recommendations as they deemed advisable.

*Professor Remington* said that the deliberations of such a board would delay the appearance of the Pharmacopœia almost indefinitely. If it could be composed of men of universal knowledge the proposition might be feasible.

*Dr. Osborne* further explained his views in regard to the proposed board, but Professor Remington was unable to agree with him that the plan was a practicable one.

*Dr. Davis* said that he was afraid Dr. Remington and others were making a bugaboo of this matter. All the drugs in the Pharmacopœia which could be considered useless were but a few in number, after all. As to the possibility of appointing a committee which could determine in a reasonable time whether or not any twenty-five drugs possess therapeutic value, one could be selected which could come to such a decision inside of twenty-four hours. It would be an easy matter to pick men of standing almost anywhere to serve on the committee. The drugs which were dropped could still be used, although no longer official. If a committee, instead of writing all over the country for advice, would undertake to decide such questions for itself, it would accomplish all that could be desired in a comparatively short time, and the settlement would be just as satisfactory as if it had occupied months. The Pharmacopœia should contain only drugs of recognized value. He did not believe that a substance could properly be called a drug unless it possessed physiological activity, and drugs alone should appear in the Pharmacopœia.

*Professor Remington* referred to Tully's powder as an example of a preparation which enjoyed only a local use. It originated with physicians in Connecticut, and few elsewhere had ever heard of it. The Connecticut men asked that it be made official, and it was put in the Pharmacopœia for their benefit, as well as for all. When a group of men are disappointed because a preparation which they are accustomed to use is not put in the Pharmacopœia, or is dismissed, they complain, and demand that the product in question shall be given recognition. A group of men in one part of the country may agree that twenty-five or thirty drugs are all that are needed. One set of men has as much right to be heard as another. He did not believe that a commission could be organized whose decision with regard to the value of a given drug would be accepted by the country at large. He believed that when all opinions had been expressed we should have to make compromises.

*Dr. Barton* said that if the pharmacological action of the official drugs were given in the Pharmacopœia it would settle this whole question. If a drug were found to have no physiological activity it could readily be dropped. He asked Professor Remington how much real chance there was that the benzoates, which he had mentioned as an illustration, would be sophisticated if they were dropped from the Pharmacopœia.

*Professor Remington* replied that up to the year 1906, when the Federal food and drugs act was passed, standards were not so necessary in case of many drugs as they are now. Reputable chemists made their preparations the best that they could. They were not very particular about minor impurities, but the conditions are different now, and manufacturers are required to conform strictly to the pharmacopœial standards. It was largely as a result of the demand for drug standards that a supplement was added to the Pharmacopœia in 1905. Someone may ask, what is the harm in leaving one per cent. of cinchonine in quinine sulphate; no physician can detect the difference, and, besides, the cost of the quinine to the consumer is much increased by the expense

of removing the last trace of impurity. The fact is, however, that the manufacturer must conform to the standards for quinine sulphate set forth in the last edition of the Pharmacopœia, and they require that quinine sulphate shall be practically free from cinchonine and other impurities. Now, what would happen if quinine sulphate should be dropped from the Pharmacopœia? Some manufacturer would omit to remove sufficient cinchonine, and, as a result, would be able to sell his product at a little lower price than his competitors. Another manufacturer would follow his example, and, in consequence of such competition, the quality of the quinine sulphate on the market might suffer materially.

*Dr. Davis* said that while the Pharmacopœia should define the quality, strength and purity of drugs, he wished that it might also contain a brief statement of accepted facts relative to physiological action; for it ought to contain pharmacological as well as chemical and physical standards.

*Dr. Stewart* asked Dr. Kebler what would actually be the effect of dismissing a drug from the Pharmacopœia, so far as the food and drugs act was concerned.

*Dr. Kebler* replied that it would have little or no effect in most instances. In certain instances it has been the custom to turn to the standards which were in force when the drug was last official, and so far this practice has been upheld. How it will work out in the States remains to be seen. Saffron is an illustration in point. It was official in the Pharmacopœia of 1890, but was dropped from that of 1900. It is very frequently adulterated, and in dealing with it the standard of 1890 has been employed. Such standards have not been found entirely satisfactory, however, and it has been found necessary to supplement them. While this method has given fairly satisfactory results, there is no question but that the addition of drugs to the Pharmacopœia has a wholesome effect upon manufacturers and dealers. When a drug is described in the Pharmacopœia, manufacturers and producers make an earnest effort to comply with the official standards for the article in question, and but little trouble has been encountered in enforcing the law in these cases. The difficulty comes in, however, when the manufacturers are given the leeway of adding impurities and then declaring their own standards of quality, strength or purity upon the label. Colocynth is an example. The Pharmacopœia requires that the seeds shall be excluded from this product. The manufacturer labels his product, which consists of colocynth with a greater or less proportion of seeds, "Colocynth Apple" or "Colocynth Powder," and then claims that it is properly labelled because these articles are not described in the Pharmacopœia under these names. The omission of some drugs from the Pharmacopœia would undoubtedly result in a great confusion of standards. Alcohol is an example. The omission of others would result in a material deterioration in quality. Quinine sulphate has already been mentioned in illustration. The omission of drugs from the Pharmacopœia also gives homœopaths, eclectics and others a chance to petition Congress for a recognition of their remedies. They all have friends in Congress and are constantly urging that their so-called standards shall be legalized. Such action, if taken, would result in a deplorable confusion of standards. Personally, he believed that twenty-five or thirty drugs were sufficient for the everyday needs of the physician, but from what had been said it was clearly evident that a much greater number should be described in the Pharmacopœia.

*Dr. M. G. Motter* said that it would be impossible to arrive at a rational basis for admitting or dismissing drugs from the Pharmacopœia until a conclusion had been reached with regard to the scope of the work. If it was to be published for physicians, that was one thing; if it was intended to furnish standards for the use of the Government, that was another. He then called attention to a method which is being employed in an endeavor to arrive at conclusions as to the composition of the next Pharmacopœia. Professor Hallberg started out to compile a million prescriptions of physicians, with the object of ascertaining what drugs are used by them and the extent of their use. He has succeeded in getting together one hundred and seventy thousand, taken in blocks

of a thousand from the files of different pharmacists. In the speaker's opinion this method was open to severe criticism. Such blocks can, as a rule, be obtained only from city pharmacists; the prescriptions will cover only a comparatively brief period of time, and it may readily happen that they are collected at a time when some particular drug is having an unusual sale, temporarily, owing to a spasm of activity on the part of advertising agents. Hence this method is liable to give misleading results unless exceptional precautions are taken. If it were possible to collect a million prescriptions under ideal circumstances there would be less objection to the method, but under existing conditions he did not believe that physicians' prescriptions would afford a valid basis for conclusions relative to the make-up of the next Pharmacopœia.

*Dr. Stewart* said he agreed with Dr. Motter. Much of the demand for remedies, particularly new remedies, is due to the advertising efforts of manufacturers. Thus, while antipyrine was protected by copyright, the product was extensively advertised and sold, but after the patent rights expired it was no longer advertised, and as a result its sale almost ceased.

Dr. Van Rensselaer said that the discussion had brought out one point very clearly, namely, that pharmacists and physicians look at the Pharmacopœia very differently. The physician regards especially the physiological and toxic action of drugs; the pharmacist, the matter of standardization, purity, etc. If a product has no physiological action it has no particular interest for the physician as a drug. In his opinion, such substances should not be given a place in the Pharmacopœia, and those which are at present official should be dropped. Their retention interferes with the usefulness of the book as a guide for students, inasmuch as it is liable to convey a misleading impression with regard to the value and usefulness of the drugs it contains.

# WHAT CONSTITUTES A USEFUL DRUG, AND SHALL THE PREPARATIONS OF A USEFUL DRUG BE LIMITED TO ONE OR TWO?

By JAMES M. ANDERS, M.D., LL.D.,
Professor of Medicine and Clinical Medicine in the Medico-Chirurgical College, etc.,
PHILADELPHIA, PA.

THE question, "what constitutes a valuable drug?" is one that can never be settled to the satisfaction of every practitioner of medicine. Much will depend upon the viewpoint of him who attempts to answer it. For example, certain writers approach the subject almost exclusively from the standpoint of the results of animal experimentation, while others base their deductions principally upon the results of clinical observations. Unquestionably, however, a most careful and judicious balancing of the facts and data derived from both of these sources (empirical observation and animal experimentation) will lead to the most trustworthy conclusions.

If one tries to imagine a race of human beings emerging from the primitive conditions of life that preceded the beginning of civilization, and looks upon its existence as something apart from all other life in its own universe; if one tries to imagine the terror with which this race regards the cessation of life, and its attempts to prolong it by whatever means; if one can imagine the conditions of education and enlightenment that existed in the early centuries of our own era; he can, perhaps, understand how much a substance as "Huile des petits chiens" could find a place in the French codex and "Magisterium cranii humani"[1] as a specific in the cure of most diseases of the head, falling sickness in particular, could be admitted to the British Pharmacopœia. With the increase of knowledge, the recession of superstition, the lessening of prejudice, and the emancipation from dogmatism, come the suggestions of a Darwin. Human life begins to be compared with all other life, and the necessity for the use of concoctions of mysterious herbs gathered at a certain phase of the moon, of chemical substances of questionable origin and uncertain action, and of animal products of disgusting sources, disappears.

The medical profession is learning slowly the benefit to be derived from sunshine, rest, fresh air, bathing, water-drinking, muscular exercise, and sleep, and, as well, the harm which comes from administering drugs for the relief of each new symptom as it arises. The profession is fast appreciating the fact that an acute infection cures itself, provided that the resistance of the patient can be maintained and that a chronic disease may be retarded in its development and progress by improved physiological conditions. The administration of drugs should, then, be undertaken, as a rule, only when some known physiological abnormality in the patient can be corrected by the use of a substance known to have a definite physiological action as the result of animal experimen-

[1] Pharmacopœia Londinensis, by William Salmon, 1691.

tation. While it is true that many drugs do not affect man and the lower animals similarly, there are known laws which intelligibly explain these variations in their action. Unfortunately, the way in which medicinal agents promote a cure of disease by this method is not exempt from obscurity and imperfections, since, under conditions of morbid processes, elements must be taken into account that differ from those observed in purely physiological operations. Although the correctness of this statement must be conceded, it is undeniably true that it is by means of experimental observation in a broad sense that practically all substantial progress in therapeutics has been realized. The more definitely the action of drugs upon the healthy organism of man and of the lower animals is determined by the experimental method, the more intelligible must become their remedial operation in disease. Such knowledge furnishes the safest guide to new applications of old remedies, and also the facts upon which therapeutic principles can be reliably based. In order to be able to determine with accuracy the precise sphere of usefulness of a given remedy, a knowledge of the cause and pathology of the morbid process it is intended to combat is a prerequisite. It has been well said that "every advance in pathology is rapidly followed by a corresponding advance in therapeutics" (Wood). Again, those drugs which destroy the causative organisms of diseases are obviously of undoubted value—are specifics. Next in point of therapeutic value come the agents that have the power to prevent fatal exhaustion, *e.g.*, in infections such as dysentery and typhoid fever, diseases for which we have as yet no sovereign remedy. Of such are strychnine, digitalis and alcohol, which ofttimes bridge life over brief periods of imminent danger, or until the specific poisons have spent their forces, and convalescence can occur. Experience has shown that the active principles of crude drugs have a much more definite and certain physiological action than the drug in its natural state, and are, therefore, as a rule to be preferred. If this conception be accepted, then the preparations of a crude drug should be limited to a very few, in most cases, at least. On the other hand, in certain of the crude drugs, with the chief active principle are associated other substances, which may modify its action, or in specific instances are essential to the production of the best results.

The question arises here, shall we abandon drugs which are advocated upon the strength of empirical observation alone? For example, should the profession have refused to employ quinine in the treatment of malaria until after the discovery of the plasmodium and the proof that a solution of quinine will kill that plasmodium? By no means; but we should demand that the bedside observations upon which we base our conclusions that a given substance is of value in the treatment of a certain disease should be extensive, and that they should be conducted by men equipped with mental powers of such a nature that their conclusions are logical and dependable. Such men should be skeptical, suspicious, painstaking and thorough in their investigations and in their analyses. The advantages in various conditions, especially those in regard to whose essential nature we are ignorant, of a considerable number of remedies, are so obvious and have been noted in such a vast number of instances that they are accorded a conspicuous position in empirical treatment. For example,

the salicylates are universally employed in rheumatism, although the *modus operandi* of their therapeutic action is wholly unknown. However earnestly the medical profession may strive to increase the knowledge of therapeutics on the basis of experience, the results of the method must be ever lacking in scientific accuracy. Conversely, a reliable, clearly defined, systematic knowledge of the curative virtues of drugs can be acquired only by means of the application of laboratory methods and the study of their influence on the sound human organism and on the lower animals.

The usefulness of the drugs and chemicals which go to make up our present-day Pharmacopœia have in the majority of instances been carefully studied by many observers in widely scattered centers of research. The observations of these investigators have been compared, their conclusions critically analyzed, and the knowledge thus gained is accessible to all who care to have it. Such remedies, true and tried, having survived the fashion of the day, are to be employed, and, because in a certain case a certain drug fails, the blame is not to be put on the drug (unless it be a poor or adulterated one), but upon an animal physiology that no longer responds to the accustomed agent in the accustomed way. These are not to be displaced by materials of wierd nomenclature, advocated by enthusiasts, upon insufficient evidence. It is self-evident that due allowance must be made for the idiosyncrasies, age, sex, temperament and acquired habits of individual patients. On the other hand, studies of the action of certain drugs of good reputation and long use have shown that the claims made for them are not borne out on the experiment table. The pathological process of the disease for which they are advocated may be of such a nature that it is absurd to expect any drug to have an influence. Such materiæ medicæ should be discarded. Naturally, it is necessary to employ solvents, diluents, flavoring agents and excipients, and these are all of value, but are not to be considered as remedial substances.

A valuable drug, then, is, 1, one that has a definite physiological action, which is applicable to the relief of a disordered physiological process; 2, one that by repeated careful clinical observations has been found to be followed in the majority of instances by a definite clinical result, care being taken to exclude the influence of accessory circumstances, and, 3, one that is used for the purpose of diluting a substance of too great concentration or making palatable an otherwise disagreeable remedy. In accordance with the definition given above as to what constitutes a valuable drug, it has seemed to me that the following, among other agents, should be omitted from the official remedies to be found in the U. S. Pharmacopœia: anthemis, berberis, calamus, calendula, cassia fistula, chimaphila, chirata, chondrus, cypripedium, eriodictyon, eugenol, eupatorium, fluidextractum berberidis, fluidextractum calami, fluidextractum chimaphilæ, fluidextractum chiratæ, fluidextractum cypripedii, fluidextractum eriodictyi, fluidextractum eupatorii, fluidextractum frangulæ, fluidextractum geranii, fluidextractum grindeliæ, fluidextractum lappæ, fluidextractum matico, fluidextractum mezerei, fluidextractum rubi, fluidextractum sabinæ, fluidextractum staphisagriæ, fluidextractum tritici, fluidextractum viburni opuli, frangula, geranium, gossypii cortex, gossypium purificatum,

granatum, grindelia, hedeoma, lappa, manna, marrubium, mastiche, matico, matricaria, mezereum, myristica, oleum betulæ, oleum coriandri, oleum hedeomæ, oleum myristicæ, pilulæ aloes et mastiches, pimenta, prunum, rubus, sabina, safrolum, staphisagria, styrax, tinctura calendulæ, triticum, ulmus, viburnum opulus, xanthoxylum and zea. On the other hand, among unofficial substances that might be advantageously added to the U. S. Pharmacopœia are diacetylmorphine and silver vitellin.

# FURTHER CONSIDERATIONS OF THE UNITED STATES PHARMACOPOEIA.

By M. H. FUSSELL, M.D.,
Assistant Professor of Medicine, University of Pennsylvania,
PHILADELPHIA, PA.

In an article published in the *Journal of the American Medical Association* for February 6, 1910, the writer pointed out certain articles that he saw fit to class as useless or obsolete drugs, and formulæ of other drugs which he thought should be excluded, mainly because they *are* formulæ. Much criticism has been offered of this article, on the ground that drugs which I chose to call obsolete are of the greatest value. For instance, one critic writes, "phytolacca in some forms of diphtheritic throats and in rehumatism is of the greatest value." Again, calendula, "when indicated and for torn lacerated condition of the flesh is the greatest antiseptic known." It is exactly because such drugs as these have no value in medicine, as shown by long experience, though doubtless most of them are harmless, which caused the article mentioned to be written by me. It seems to me that accurate knowledge of the causes of disease and of the pathology of diseased conditions is now so far advanced that, in order that practising physicians (of whom I am happy to say I am one) may not expose themselves to ridicule, we must have in the Pharmacopœia only drugs the usefulness of which has been proven by clinical experience or clinical experience plus laboratory knowledge. It would also seem that a gentleman who uses a drug or combination of drugs for "kidney, bladder and liver troubles" is just the individual who should be impressed with what is unquestionably the fact, namely, that any therapeusis for a given condition must be based upon an accurate diagnosis of that condition.

It is unquestionably true that many of the recoveries of our patients are due not to the drugs used, but the inherent tendency of the human organism to repair. Therefore I feel that in the forthcoming Pharmacopœial Convention much stress must be placed upon the necessity of making the next issue of the Pharmacopœia a book that contains only drugs which clinical experience plus laboratory knowledge have proved to be of value. I most thoroughly believe that the entire list of drugs which I have given are useless, and hence should be expunged. Likewise, many drugs have been used since the revision of 1900 which must be included in the revision of 1910. Another point which I wish to elaborate is the presence in the Pharmacopœia of such combinations as pulvis acetanilidi compositus. Now, surely the best method of prescribing acetanilide and caffeine is to give to each individual for which these drugs are used the dose necessary for that individual, and for the particular condition present at the time the patient is seen. This cannot be done if a fixed formula is used, even though, of course, one may use different doses at different times. If the dose of the whole mixture is varied, necessarily the ratio of the various drugs continues in the same proportion; thus, the amount of acetanilide in

500 milligrammes of the mixture quoted is 35 milligrammes, and the amount of caffeine, 5 milligrammes. One might desire to give 70 milligrammes of acetanilide and 5 milligrammes of caffeine, and this would be impossible if the ready-made mixture were used. It is manifestly impossible for any one to tell before a case is seen just what dose of drug is necessary. To advise the use of compound remedies is to confirm slipshod, improper methods of prescribing. On this principle, fixed formulæ should not be used. If it is not correct principle to use fixed formulæ, then they surely should be expunged from the Pharmacopœia.

Still another point: the Pharmacopœia to-day contains certain drugs, their preparations, the method of manufacturing them, their doses, their description, and in certain instances tests for their purity and assay. As the book stands, therefore, it is manifestly of great use to the pharmacist. Its only use to the general practitioner is the knowledge it gives him of what is supposed to be useful in the line drugs and their doses. It gives no hint of their indications or contraindications, of their toxic or non-toxic properties. All this knowledge he perforce must get from other books, or from manufacturing chemists. He *can* get reliable information from the various publications on materia medica or from the dispensatories, and he does get some from these sources, but, sad to relate, most of the information as to drugs which the average physician now obtains after graduation is from manufacturing drug firms, in the form of more or less well-written literature, accompanied by samples and often supplemented by the glib-tongued detail man. The writer has had described to him the treatment being carried on in certain cases, and has been able to recognize but few of the articles used, because they were prescribed under trade names of which he was entirely ignorant. One reason why the drug firms, with their literature and instructed agents, are such potent powers in grounding the young physician as to the means he should use in prescribing is because that method is easy and is brought immediately to his attention, whereas the instruction in the materia medica is more or less difficult to attain. Another reason is because the medical schools are not insistent enough in teaching their students that the only proper method for them to pursue in prescribing drugs after they become practitioners of medicine is to hold fast to that which has been proven of value, and to accept new remedies only after their usefulness has been attested by men of standing, by methods of value.

Now, if the next issue of the Pharmacopœia is made to contain the therapeutic indications of the drugs recommended for use, it will be of some practical value to the practising physician. If this would make the volume too bulky, there might be two volumes printed; one after the style now in use, and the other to contain the names of the drugs, their description, their dose, and a short description of their therapeutic use.

# SUGGESTIONS FOR THE PHARMACOPOEIA OF 1910.

## A Brief Consideration of the Subject in its Relation to the Federal Food and Drugs Act.

BY FRANCIS P. MORGAN, A.B., M.D.,
WASHINGTON, D. C.

BY the Act of June 30, 1906, the Pharmacopœia and National Formulary were made legal standards for drug products in the United States.

Section 6 of the Act provides:—

"That the term 'drug', as used in this Act, shall include all medicines and preparations recognized in the United States Pharmacopœia or National Formulary for internal or external use, and any substance or mixture of substances intended to be used for the cure, mitigation, or prevention of disease of either man or other animals."

Section 7 reads in part as follows:—

"That for the purpose of this Act an article shall be deemed to be adulterated (in case of drugs): First. If, when a drug is sold under or by a name recognized in the United States Pharmacopœia or National Formulary, it differs from the standard of strength, quality or purity, as determined by the test laid down in the United States Pharmacopœia or National Formulary official at the time of investigation: Provided, That no drug defined in the United States Pharmacopœia or National Formulary shall be deemed to be adulterated under this provision if the standard of strength, quality or purity be plainly stated upon the bottle, box, or other container thereof, although the standard may differ from that determined by the test laid down in the United States Pharmacopœia or National Formulary."

Regulation 7 of the rules and regulations for the enforcement of the food and drugs act is based upon Section 7 of the Act, and is entitled "Standards for Drugs." It reads:—

"(*a*) A drug bearing a name recognized in the United States Pharmacopœia or National Formulary, without any further statement respecting its character, shall be required to conform in strength, quality and purity to the standards prescribed or indicated for a drug of the same name recognized in the United States Pharmacopœia or National Formulary official at the time.

"(*b*) A drug bearing a name recognized in the United States Pharmacopœia or National Formulary, and branded to show a different standard of strength, quality or purity, shall not be regarded as adulterated if it conforms to its declared standard."

Thus the Pharmacopœia, having become a legal standard for the strength, quality and purity of drugs, has assumed a close relation to the Federal food and drugs act. With comparatively few exceptions all drugs which are subject to the act, and which bear the names of preparations described in the United States Pharmacopœia, are required to conform in strength, quality and purity to the standards therein set forth. The exceptions comprise drug products which bear statements upon the label with regard to their own standard of strength, quality and purity. From this it is clearly evident that in order to secure the highest degree of efficiency for the food and drugs act, particularly

in the execution of the portion of Section 7 relating to drugs, adequate legal standards are necessary. The standards should be sufficiently high to insure a product of the greatest possible value for the purposes for which it is intended. They should not be unreasonably high, or so low as to fall short of the attainment of the objects in view. They should be clearly set forth in the Pharmacopœia in language which is free from ambiguity, and, as far as possible, not susceptible of misinterpretation.

Experience has shown that standards which at first appear to be excessively high are sometimes found by actual test to be well within the bounds of reason and possibility. When the law was first enforced in the case of asafœtida, the objection was made that it was utterly impossible to secure abroad a product of a sufficient degree of purity to conform to the pharmacopœial requirements. The legal standard was rigidly upheld, however, shipments of an inferior article were repeatedly rejected, and, as time passed, more and more asafœtida of official quality was offered for import. Hyoscyamus affords another illustration. When the attempt was first made to enforce the law in case of this drug dealers persistently claimed that it was impossible for them to secure henbane leaves of the alkaloidal strength prescribed by the Pharmacopœia. But, while samples of commercial hyoscyamus still occasionally give evidence of adulteration, examinations of the leaves offered for import during the year 1909 showed that the product had improved materially in quality and in most instances had complied with the pharmacopœial requirements.

The three years which have elapsed since the law went into effect have afforded an opportunity to test the efficiency of the Pharmacopœia as a legal standard in the case of many drugs, and, as might have been expected, instances have arisen in which the official standards have not proved all that could be desired. It is hoped that this matter will be brought to the attention of the Revision Committee in detail by the proper authorities, with appropriate suggestions for the Pharmacopœia of 1910. In the time allotted I can only indicate a few of the changes which would, in my opinion, be desirable.

The proportion of foreign matter permissible in the crude vegetable drugs should be definitely fixed. Drugs consisting of the leaves, roots and other similar parts of plants invariably contain a certain proportion of foreign material, consisting of stems, seeds, sand, earth, etc. The quantity varies with different drugs and in different samples of the same drug, and in most cases its presence is purely accidental. In some instances, however, the foreign element is intentionally added for purposes of adulteration. Whether adventitious or introduced for purposes of fraud, it is objectionable, and definite standards should be established in order that a line may be drawn between satisfactory and unsatisfactory products so far as this point is concerned. Such requirements when once incorporated in the Pharmacopœia are, as already stated, recognized under the law, and become potent agencies for the prevention of deception.

The need of such standards is seen in the case of senna. Senna is defined in the Pharmacopœia as the dried leaflets of cassia acutifolia, or of cassia angustifolia. The Pharmacopœia further sets forth a description of Alexandria

and India senna, and states that the product should be free from stalks and from argel leaves. Early examinations of commercial samples of the drug soon disclosed the fact that the senna upon the market in this country was only in part made up of the pharmacopœial product. Much of it consisted of a product whose composition can be readily understood from the following brief descriptions regarding the quality of shipments of this drug offered for importation at the port of New York: "senna siftings;" "excessive sand;" "not U. S. P. senna, but siftings containing seeds, stems, flowers, buds, earth, etc.;" "not U. S. P. senna, but dirty screenings;" "not senna, but senna siftings containing seeds, stems and flower remnants;" "adulterated with stems, seeds and sand." The percentage of ash, which indicates the proportion of inorganic or waste material present in these various samples was as follows: 35.31 per cent.; 21.73 per cent.; 16.1 per cent.; 20.5 per cent.; 14.7 per cent.; 17.3 per cent. Owing to the persistent refusal of the authorities to permit the importation of such shipments, the quality of the senna upon the market has very materially improved, but there is no definite pharmacopœial standard by which the line may be drawn between satisfactory and unsatisfactory samples of the drug in this country, so far as inorganic constituents are concerned. A definite pharmacopœial requirement with regard to the ash limit would go far toward solving the problem. This suggestion applies also to conium and ipecac, both of which have been found adulterated with powdered olive stones; to kamala, samples of which have been found to be heavily adulterated with sand; to belladonna, stramonium, digitalis, licorice, cubeb, buchu, calendula and taraxacum, and to the crude vegetable drugs in general.

The experience of the last three years indicates that from the standpoint of the efficiency of the food and drugs act the addition of powdered vegetable drugs to the Pharmacopœia is desirable. Colocynth, for example, is defined by the Pharmacopœia as the peeled, dried fruit of citrullus colocynthis deprived of the seeds. In the light of this definition there should be no difficulty in determining what constitutes powdered colocynth. As a matter of fact, however, the question has given the authorities much trouble. Samples of powdered colocynth taken for investigation have repeatedly been found to consist of official colocynth mixed with a variable proportion of powdered seeds. When the matter has been brought to the attention of the dealers they have in most instances claimed that the shipment into interstate or foreign commerce of a powdered colocynth consisting of fruit and seeds constitutes no violation of the food and drugs act, because powdered colocynth is not described in the United States Pharmacopœia, and there is consequently no legal requirement with regard to the quality or purity of this article. The addition of powdered colocynth to the Pharmacopœia, or, better, the incorporation of a general statement to the effect that the powdered drug must in all cases consist of the powdered official crude drug of the same name, would do much toward increasing the efficiency of the Pharmacopœia in this direction.

Experience in enforcing the law in its relation to hyoscyamus has shown that the requirements with regard to this drug should be more definite in one particular at least. Hyoscyamus is defined in the Pharmacopœia as "the dried

leaves and flowering tops of Hyoscyamus niger Linné (Fam. Solanaceæ), collected from plants of the second year's growth, and yielding, when assayed as directed below, not less than 0.08 per cent. of mydriatic alkaloids." The wording "of mydriatic alkaloids," without further specification as to name or kind, affords a loophole of escape for those who desire to evade the law. Much of the commercial henbane examined has been found to be adulterated with stramonium, a weed containing mydriatic alkaloids. Considerable difficulty has been encountered in enforcing the law in the case of hyoscyamus so adulterated when the presence of hyoscyamus leaves or tops could be established only with difficulty by microscopical or other means, as, for instance, in fluid preparations and extracts, and especially in cases where the total percentage of mydriatic alkaloids present equalled or exceeded the required 0.08 per cent. From this it would appear that the requirements of the next Pharmacopœia relative to hyoscyamus should, if possible, be made more specific with regard to the particular mydriatic alkaloids which official hyoscyamus should contain. This suggestion also applies to belladonna, which is sometimes adulterated with scopola leaves and poke root, and to stramonium.

The Pharmacopœia defines copaiba as "an oleoresin derived from one or more South American species of copaiba." The present requirements for this drug are fairly satisfactory so far as they go, and the quality of the copaiba upon the market is constantly improving. The chief difficulty encountered in enforcing the law as it relates to this product concerns the source from which copaiba is derived. In addition to South American copaiba, many shipments of the African variety, an inferior product, have come to this country. To distinguish between the two by the tests laid down in the present Pharmacopœia is a difficult matter. Methods by which they can be readily differentiated have been worked out, however, and the question whether or not such tests should not appear in the next Pharmacopœia is one for the Committee of Revision to determine. This suggestion applies also in a way to the balsam of Peru, great quantities of which are annually imported to this country. The object of standardization in case of this drug would be to facilitate the differentiation between the pharmacopœial product and an imitation product which is being offered for import, and which can be distinguished from the pharmacopœial product by present methods only with difficulty.

When the law went into effect it was found that large quantities of saffron were coming to this country loaded with glycerin and oils or inorganic substances like potassium nitrate, or heavily adulterated with calendula flowers and colored with coal-tar dyes. Saffron is not official in the present Pharmacopœia, but it appeared in that of 1890. The authorities took the position that under the circumstances saffron should at least conform to the requirements prescribed for this drug in the last Pharmacopœia. The dealers, when notified to this effect, at once raised strenuous objection, claiming that there was no legal standard for the strength, quality or purity of saffron, and that the position of the Government was not supported by law. By adhering rigidly to the position assumed, however, and by requiring shippers to conform strictly to the requirements for saffron set forth in the last Pharmacopœia, a marked improve-

ment has been brought about in the quality of the drug offered for import. Nevertheless, the addition of saffron to the next Pharmacopœia would greatly facilitate the execution of the law so far as it relates to this drug.

From what has been said it is clearly evident that, from the standpoint of efficiency of the food and drugs act, the more drugs described in the next Pharmacopœia, the better, provided that the drugs in question are properly standardized. This proviso is of great importance, however, because the presence in the Pharmacopœia of drugs without standards, or with inadequate standards, is of little or no advantage so far as facilitating the execution of the law is concerned. Inadequate standards are often worse than none. It would appear, therefore, that from the standpoint above mentioned as many well-standardized drugs as possible should be set forth in the next Pharmacopœia.

Many opinions have recently been expressed with regard to drugs which might well be spared from the Pharmacopœia. Most of them are drugs which have been found to be practically worthless in the treatment of diseases for which they were formerly employed, or which have fallen into disuse for other reasons. But, whether they are efficient or inefficient, and whether they are used by the profession or wholly by the laity, so long as they are used in this country as medicinal agents, the existence of Section 7 of the food and drugs act, to my mind, offers a potent reason for retaining them in the Pharmacopœia, provided they are furnished with adequate standards and tests as to strength, quality and purity. Furthermore, it would appear that the addition of well-standardized drugs to the Pharmacopœia is in every way an advantage to the cause of pure drugs.

# THE METRIC SYSTEM.

By ELI H. LONG, M.D.,
Professor of Materia Medica and Therapeutics, Medical Department,
University of Buffalo,
BUFFALO, N. Y.

To obtain sufficient data for an adequate estimate of the present use of the metric system by physicians in this country was impossible in the short time at disposal for preparation of this paper. It was thought, however, that data from a number of the larger cities would indicate something of present tendencies, and such will be presented.

Thirty years ago the Pharmacopœial Convention substituted "parts by weight" for the troy weights and liquid measures in the revision of the Pharmacopœia. This was a step in the direction of simplicity and it permitted the use of any kind of weights and measures. The next convention, ten years later, adopted the metric system exclusively. This course was taken because of the patent advantages of the simple decimal system over the English system, with its two different pounds and ounces and its several different gallons, and with its numerous symbols for their expression. It is not necessary to argue these advantages here, but they are just as real now as they were then, and to advocate a return to the old system would be as rational as to propose a return to the pounds, shillings and pence in money values. Granted that the metric system would be preferable if once in common use, our thought will be concerned with the reasons for its slow progress and with suggestions for its advancement.

About ten years ago Dr. Whelpley reported upon 1,008,500 prescriptions from all parts of the country, showing 6 per cent. written in metric terms. The rather meager figures here offered are hardly entitled to stand in comparison with Whelpley's million prescriptions, but they are given for what they are worth. Eighteen thousand recent prescriptions in ten of the larger cities show an average of 12 per cent. in the metric system. The most valuable facts regarding these are the comparisons made possible in any single city and the relation of increase to the teaching in the local medical school or schools. My own city presents an opportunity for such observations: In the statistics of ten years ago Buffalo reported 9.6 per cent. of metric prescriptions. Now, 4000, from six different pharmacies, show an average of 16.5 per cent. Related to this satisfactory increase is the fact that the medical school has for the past ten years required the use of the metric system exclusively in the learning of doses and in prescription-writing. The highest percentage of any city is shown in New Haven, which gives 34 per cent. in 1000 prescriptions. This is a tribute to the efforts of Dr. Osborne, who for twenty-three years has taught the system in Yale medical school. Next to this, Boston shows 26.2 per cent. of metric prescriptions among 3000 from three stores. Here, in Harvard medical school Dr. Pfaff teaches the metric system exclusively, while Tuft's College

Medical School teaches it in preference to the old system. In contrast to these figures showing progress, the opposite result obtains in some cities. Thus St. Louis, with 11.8 per cent. ten years ago, now reports 8 per cent. among 2000 prescriptions from two stores. The number of prescriptions reported upon in any case, however, are too few to be taken without reserve. The fact is that figures will easily vary even in different parts of the same city. Still, it is noticeable that some of the largest cities are very backward in the use of the metric system. From one of the large medical schools in New York City comes the opinion that it is used very little there, and from Philadelphia comes the estimate, based upon information obtained from several leading pharmacists, that only about ½ of 1 per cent. of prescriptions in that city are in metric terms. Noting the relation of this estimate to the attitude of the medical schools, I find that the two largest schools in that city give the metric system only a subordinate place in their teaching.

Because of the important relation of the medical schools to the matter, the present inquiry was extended to about 50 of the representative schools, in order to ascertain to what extent they employ the metric in respect to doses and prescription-writing. Replies from 40 schools give the following showing:—

| | |
|---|---|
| Metric system taught exclusively, in | 6 |
| Metric system taught in preference to the old system, in | 8 |
| Metric system taught equally with the old system, in | 14 |
| Old system taught in preference to the metric, in | 12 |
| | 40 |

Thus only 14 out of 40 medical colleges give preference to the metric system. Considering the advantages admitted for it and the fact of its being the official system in our national standard, I submit that the medical schools are not giving the metric system a fair trial.

Now, what are the chief hindrances to its more rapid adoption in practical prescribing? In view of the influence of the teacher upon the thought and later practice of the pupil, we must hold the apathy of medical teachers to be mainly responsible for the slow progress made. Teachers in therapeutics are not entirely to blame, for in some schools the new system is taught in the earlier years, but this teaching is neutralized by the practice of the clinicians who teach and write prescriptions in the old system. The same influence is likely to continue through the period of hospital interneship, through use of the old system in the hospital. Another influence is that of the manufacturing houses, who use the old system exclusively upon their labels. This favors neglect of the new system even by those who had previously learned to use it.

From one of our largest Eastern cities comes the opinion of several pharmacists to the effect that the majority of apothecaries in that city are not competent to properly dispense metric prescriptions, some because they do not have the metric weights and measures and others because they do not understand it. This statement of opinion from a medical center, twenty years after the adoption of the metric system by the U. S. Pharmacopœia, is surprising. It is incredible that such a statement of conditions can represent more than a limited locality, for the colleges of pharmacy are using the U. S. Pharmacopœia

extensively and are teaching the metric system. I venture the belief that, as a rule, the pharmacists of our cities are in advance of the physicians in readiness and ability to employ the metric system. If they are not equipped it is because the practice of physicians has not demanded it.

As to the wisdom of continuing to teach the metric system, this question can most properly be answered by those teachers who have given the system a fair trial, who for a decade or more have given it at least an equal place with the old system. Those who have subordinated it should begin to use it in earnest, so as to be ready to discuss the matter ten years hence in case it should be a live question then. As an indication of the probable result of such trial, a reference to the replies from medical colleges shows that, out of 40 teachers replying, the 28 who teach the metric system either exclusively or equally with the old system seem satisfied with their plan. At any rate, in answer to a direct question as to any probable change of custom, not one indicated any desire to discontinue the metric system, while several express a tendency toward a larger use of the same.

Now, assuming that it is desirable to propagate the use of the metric system, what are the most efficient means of so doing? We can expect to do little among the rank and file of practitioners outside of the schools and hospitals; but, with the majority of schools now teaching it upon a par with the old system, if we could interest clinical teachers to the extent of adopting the system for the sake of the advance it would mean, its continued use by beginners would be encouraged and aided. A discussion of methods of teaching the system, and an exchange of experiences by teachers, would stimulate effort. The manufacturing houses could aid by adding metric quantities upon their labels. The use of approximate, rather than exact, equivalents has been advocated with good reason. These and other means must, however, be subordinate to teaching and practice of the system in the medical schools. Adequate correction of the proprietary evil requires that our students be more thoroughly taught in practical prescription-writing, and the report of the Sub-committee on Pharmacology, of the Committee of One Hundred, emphasizes the need of prescription drills for advanced students. In carrying out such a plan an excellent opportunity is afforded of requiring the student to become practically familiar with the metric system by using it exclusively in these exercises.

But, after all is said as to the desirability of the system, there remains great practical difficulty in attempting to write prescriptions in the new system when one is obliged, from long usage, to think in terms of the old. This difficulty, however, can be easily overcome by use of a simple rule[1] that will enable anyone, no matter how firmly tied by custom to the old system, to at once write his prescriptions in the metric system without the necessity of calculating quantities and with less expenditure of energy. If you will permit its rehearsal, it may be stated that it involves ordering the number of doses that represents the multiplier in converting grammes to grains, *i.e.*, 15 (16 for

[1] Medical News, Philadelphia, March 25, 1893.

liquids); then the number that expresses the single dose in grains or minims will express the total quantity in grammes or cubic centimeters. For example:—

| | Gm. or c.c. | |
|---|---|---|
| ℞ Potassii bromidi (single dose 10 grains) ..... | 10 | 25 |
| Morphinæ sulphatis (single dose ¼ grain) ..... | | |
| Spiritus ætheris nitrosi (single dose 30 minims) ..... | 30 | |
| Aquæ cinnamomi, q. s. ad (16 teaspoonful doses) ..... | 60 | |

M. Sig., etc.

The formulated rule is as follows:—

1. Make the whole quantity to consist of sixteen doses (15 for solids); then

2. The number that represents the single dose of an ingredient in grains or minims will express the total required quantity in grammes or cubic centimeters.

While such a rule may be regarded as a prop, its use will mean economy of time and energy to the man now writing his prescriptions in the old system.

In conclusion, it would seem that the American Therapeutic Society should place itself upon record in favor not only of a continuance of the present official system of weights and measures, but of a propaganda with the object of securing its more general use by physicians. It may be that this Society is the proper body to conduct such a propaganda.